FIFRA SCIENTIFIC ADVISORY PANEL (SAP)

OPEN MEETING

AUGUST 28, 2002

VOLUME II

Located at: Sheraton Crystal City Hotel
1800 Jefferson Davis Highway
Arlington, VA 22202

Reported by: Frances M. Freeman

C O N T E N T S

DR. PORTIER: Good morning.

I would like to welcome you to the Science Advisory Panel Meeting for Wednesday, August 28th.

This morning's meeting will focus on corn rootworm plant incorporated protectant non-target insect and insect resistant management issues. Today's focus will be on insect resistant management issues.

I'm Chris Portier; I'll be chairing this FIFRA Science Advisory Panel meeting this morning. I would like to begin the meeting this morning by having the panel introduce themselves, a brief description of where they are from and what their expertise is and today we'll go backwards.

So we'll start on the far side with Dr. Whalon.

DR. WHALON: Thanks.

Mark Whalon, Michigan State University. I'm an Applied Insectocologist with history of working in insect resistant management.

DR. NEAL: Hello. I'm Jonathan Neal

from Perdue University. I am an Insecticide Toxicologist with experience in western corn rootworm resistance to crop rotation.

DR. HUBBARD: Bruce Hubbard. USDA ARS, Columbia, Missouri. I work with -- have been working with corn rootworm since 1985, currently run a large breeding program for native host plant resistance, as well as working on the ecology of the insects applicables to insect resistance management such as larva movement and alternate hosts.

DR. CAPRIO: My name is Mike Caprio. I'm from Mississippi State University. I'm a Population Geneticist and Modeler, looking at insecticide resistance management.

DR. ANDOW: I'm Dave Andow, University of Minnesota. I'm an Ecologist in the Department of Entomology. I have been doing work in modeling and monitoring associated with insect resistance.

DR. WEISS: I'm Mike Weiss, University of Idaho. I have about 15 years of experience in applied corn rootworm management.

DR. GOULD: Fred Gould, North Carolina State University. I have been working on ecological genetics of insect adaptation to control measures, specifically also on resistance management, both empirical work and modeling.

DR. FEDERICI: I'm Brian Federici, from the University of California at Riverside, Department of Entomology. I'm an Insect Pathologist; I work on the molecular biology of cry proteins and their synthesis and the design of recumbent bacterial insecticides.

DR. HELLMICH: Rick Hellmich from the USDA ARS, corn insects and crops and eggs research at Ames, Iowa. I'm an Insect Ecologist. I've been working with insect resistance management issues with European corn bore and also non-target issues with Bt corn.

DR. PORTIER: As I mentioned, I'm Chris Portier; I'm Director of the Environmental Toxicology Program at the National Institute of Environmental Health Sciences. I also manage the US National Toxicology Program. My area of expertise is in statistics as applied to environmental health issues.

Welcome, all of you. Thank you for your time for being here today.

I would like to now turn the mike over to Mr. Paul Lewis, the Designated Federal Official to cover some administrative issues.

Paul.

DR. LEWIS: Thank you Dr. Portier.

I would like to again thank Dr. Portier for agreeing to serve as our chair for this meeting over the next two days and for also thanking the panel members for their time preparing for this meeting and the upcoming deliberations.

As I mentioned during my opening remarks yesterday, my role as designated Federal Official is to ensure this meeting follows the Federal Advisory Committee Act and again with that in mind, this is an open meeting. All materials are available in the public docket.

We will also write a report that serves as meeting minutes that will capture discussions by the panel during the course of the next two days.

This report will be available in approximately 4 to 6 weeks posted both on our SAP web site, in addition to be available in the OPP docket. Thank you I'm looking forward to some very challenging deliberations over the next two days.

Dr. Portier.

DR. PORTIER: Thank you Mr. Lewis.

Now, a welcome by Ms. Sherry Sterling, who is the Acting Director of the Office of Science Coordination and Policy.

MS. STERLING: Good morning.

On behalf of the Office of Prevention Pesticides and Toxic Substances, I would like to welcome you and also to say thank you.

As I mentioned yesterday, I know there is so much work that goes on with the panel members.

It isn't just what we see in front of us in the discussions here, but it is the work that goes on in preparation for the meeting and for us also, very importantly, the report writing that goes on after the meeting.

So for this, for what has happened already and for what is to come, thank you very much.

These issues before us are important ones and interesting and in all areas and facets of society, they are of interest.

And so to keep it on the scientific plain, it is sometimes difficult, but I know that you all will be able to do that.

And we are very interested in hearing what you have to say from a scientific perspective. It helps guide us in making decisions and keeps us on the right path.

Hearing from many different perspectives only can help to improve the work that we produce and it is -- what we do is science-based, I can assure you of that. So, it is very important to us.

Marcia Mulkey couldn't be here with us today. She is the Director for the Office of

Pesticide Programs, but she does send her regards and also joins me in thanking you for the work that have you done here and are doing here.

So thank you and I like look forward to a productive two days. Thank you.

DR. PORTIER: Thank you Ms. Sterling.

Dr. Andersen, is there something you want to say before we go to finish up from yesterday's discussion?

DR. ANDERSON: I just would like to also add my comments for Marcia Mulkey who could not be here today and say I can't do it as -- probably as eloquently as she did, but yesterday she talked about how important it is for public service.

We who are federal employees on a regular basis know this and understand it and we appreciate that you will take time -- some of you on a temporary basis there are some of you who are permanent federal employees also -- but take the time to give the public service to us.

We think that this is incredibly important to us and we really do appreciate that you are doing that. I think -- do you want me now to introduce my panel for today?

DR. PORTIER: We'll come back.

DR. ANDERSON: Okay. We'll come back. Thank you.

DR. PORTIER. Thank you, Dr. Anderson.

Yesterday, we had a SAP meeting. The focus of that meeting was on non-target insect issues associated with the corn root plant incorporated protectant, Cry3Bb1.

Question two from yesterday involved a little more detail than we had time to get into during the panel discussion. A subgroup from yesterday's panel debated some of the issues associated with question two last night and they were asked to come to us and report this morning on their discussions.

So, we will do that now. I will note for the record that this is a subgroup of the panel. It does not -- it is not the recommendations of the entire SAP panel that was here yesterday, since that panel is no longer here, but it is something that we think was important from yesterday's meeting and we do want to hear about today.

For the record again I will repeat the question we were looking at yesterday so that you have some context of what we were talking about.

The question was, "Please comment on the adequacy of the two-year field abundance study for making a determination of the potential risks from commercial use of event MON 863."

Dr. Federici, who was in that subgroup, will present their comments this morning.

DR. FEDERICI: Thank you Dr. Portier.

What I would like to do is prior to -- to understand the perspective, I'm going to layout for you here, I want to just read the statement that precedes the question as it was given to this and that's under question two, duration of field abundance studies and then there is two statements made there.

The first is, "A two-season field invertebrate abundance study indicates that MON

863 corn does not have a negative impact on the abundance of non-targeted invertebrates."

The second statement is, "Data also indicated that planting event MON 863 results in less impact on non-target invertebrates than conventional past management practices." Overall I would say, we do not think the study that we were supplied with is adequate to answer the question. So, that's kind of our overall summary. That's kind of our overall summary.

I want to point out a few things here. The first is that we -- the data we have is really only for a one-year study. It is not for the full two-year study. So, there may be other information that is available at this point, but we do not have that. We only have the data from the first year.

The second thing is that in contrast to this statement, data also indicated that planning event MON 863 results in less impact on non-target invertebrates than conventional past management practices. We do not find that the data support that statement.

So, we found basically -- and this is actually the conclusion of that study in the first year as mentioned in that report is they found no significant differences in most of the treatments. There were few cases like with spiders where with foliar application there was -- there were significant differences.

But in general, the Monsanto Report itself concludes that there are no significant differences among most of the treatments.

So, we don't think that -- now, to look at from it the standpoint of risk, we do not think that the data we were supplied with is adequate at all for assessing risk. There might be some information in the report that would indicate some utility for the assessment -- for assessing hazards.

We also think hazards could probably initially, be more assessed in a laboratory study that focused on something like -- some of the main insects are you interested in. For instance, the carabid beetles.

So rather than go on at length, I want to just summarize some of the key points, some of the things we thought that might be looked at in future studies and I will give you a list of these.

But I'll just summarize them briefly here to really -- with a focus on improving from what we think you want to know, the types of study that might be done. I'll just summarize these here.

State clearly the number of back cross generations that separate MON 863 hybrids from the non-Bt Control. That's the RX 670 line. Add additional plus Bt versus minus Bt hybrid to the study. Include a highly toxic, gut active insecticide to act as a positive control, one that would replace force.

Along with that, in monitoring -- in doing the actual sampling in the field, we think that the actual sampling could be better synchronized with the insecticide treatment so that you had an -- an immediate pre-count before the insecticide treatment was made and then do follow-up studies one day after, three days after, four days after and maybe limit these to only one-day rather than three-day periods of sampling.

Consider eliminating the pounce treatment. If the epigenol (ph) fauna is being studied, see the alleles between the plots with vegetative cover to reduce enter-plot movement of thing such as the carabids, which will -- with a plot size -- with the replicates that they were using -- it's from the people who are knowledgeable of the carabids, they can move between these plots pretty efficiently.

Maintain alleyways of at least 20 feet between all plots, not just the replicates.

Edge effect should be minimized, using the same variety as in the Bt plots. Eliminate root ball samples or increase the number per plot to about ten.

So, in other words, either increase it so you have good statistical power there or you eliminate that kind of test if you don't really think it's relevant.

Increase pit fall traps to at least at ten. The way they did the study, they had four, but in some of the replicas actually, they only had -- only two were actually sampled. They didn't have the full numbers. So, we think the -- and focus these toward the -- have these concentrated more in the center of the plot. So, increase those -- Ten was maybe a maximum. Maybe you could get by with a lower number. Consider adding whole plant visual samples greater than 50 per plot. Eliminate drop cloth method.

This is a good preliminary method but less suitable for quantitative analysis and analyze and interpret the data only for those species that are sufficiently abundant. That sampling precision is much less than mean density. I think that's a very important point.

So, that basically is a summary of our comments. We'll expand on these a little in the written but those are the key points we wanted to make. We do not consider -- the bottom line is we do not consider this particular study that we were given adequate for the assessment of risk.

DR. PORTIER: Dr. Andersen, Ms. Rose do you have any questions for clarification?

MS. ROSE: The only thing I didn't hear you mention is appropriate plot size or minimum plot sizes.

DR. FEDERICI: Minimum plot size? We --

MS. ROSE: When are you talking about 10 samples you can't -- I mean, I think some of these 24 rows --

DR. FEDERICI: This is for the traps within the plot. I think there is an agreement that the 60 by 60 is acceptable.

MS. ROSE: I acceptable. Okay. Thank you.

DR. ANDOW: I don't think there was entire agreement. I think that some of us, including myself, felt it was adequate but others felt it really needed to be larger.

DR. PORTIER: That was in the larger

discussion yesterday.

DR. FEDERICI: I think there was some sense that some of the actual plot sizes are limited by the EUP in terms of the amount of material they can actually have out there and maybe even when this study was done, by the amount of seed that was available so that ultimately -- I mean, you are asking us to answer with whether this particular study was adequate, that these types of studies, we think, would be effective in answering, maybe your question.

Once there are larger plantings out there and have you larger plant plot sizes -- where again, you would have, depending how you do the sampling, better statistical power.

DR. HELLMICH: I would like to follow up on that --

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: I was involved in these discussion. We may want to back up a little bit first.

I know there is societal pressures to

evaluate these new products. I hope we don't get our hopes and expectations for assessing these products to exceed what the science is.

There are problems with scale and some of us believe that the questions that you asked Monsanto to address may have been impossible to answer, given the limitations of seed availability and even some of the scale issues.

And I think that is a very -- it is a serious question that we need to consider given that there is several researchers across the United States through doing experiments very similar to this right now. There certainly needs to be discussion on the appropriateness and the scale and of course the seed availability for these type of experiments.

So, the bottom line is as you may have asked Monsanto a question that was impossible to answer.

DR. PORTIER: Dr. Andow, briefly.

DR. ANDOW: Related to the plot size issue, there was some debate as to what the purpose of the experiment was.

And it seemed to have been designed to look for the insecticide affects in which case the insecticide affects were expected because of the way it was split and the emphasis on the -- with the power associated with the insecticide treatments rather than Bt treatments.

So the insecticides affects were expected to be temporary. Under those circumstances, I think the analysis of one of the members of the subgroup was that those temporary affects probably could not be detected in a 60 by 60 foot plot.

Persistent defects that result from the treatments might be able to be detected on 60 by 60 plots. But the problem with the smaller plot size is if you don't detect a difference, it could be because the difference was swamped by the movement between the plots.

So, it sort of gives you a situation where you really are in a position where you can't say that nonsignificant differences imply that there isn't an effect.

DR. PORTIER: I think some of that was part of yesterday's discussion and will appear in the regular report.

Given that, then, we'll move forward a little bit.

Dr. Andersen, before I turn it over to you, I'm going to ask Ms. Thrall on my left to introduce herself. Dr. Thrall.

DR. THRALL: Good morning, Mary Anna Thrall. I'm a Veterinary Pathologist at Colorado State University.

DR. PORTIER: Thank you Dr. Thrall.

Dr. Andersen, tell us about insect resistance management.

DR. ANDERSEN: Actually, I will let the staff do that.

To my immediate left is Robyn Rose who will be making the presentation. Then Dr. Sharlene Matten, Alan Reynolds and Phil Hutton. Phil is actually the Branch Chief for the Micro Pesticide branch that has these products under his jurisdiction, essentially.

Alan and Phil especially, will be helping us with some of the electronics as we go forward today. So, we're hoping it all works, as I mentioned to Chris.

We had a little bit of excitement in our building. We had a fire or fire drill or something like that this morning at a quarter of eight so, we're hoping we have everything now set up and ready to go. We'll see how it goes.

So, with Alan's assistance, if you give us just a minute, we'll turn it over to Robyn to begin.

DR. ROSE: Good morning. My name is Robyn Rose. I'm an Entomologist with the Office of Pesticide Programs, Biopesticides and Pollution Prevention Division.

Today I will be giving a brief summary of EPA's preliminary review of Monsanto's Interim Insect Resistance Management Plan for Bacillus thuringiensis Event MON 863 Corn Rootworm Protected Field Corn.

This is a preliminary review which will be finalized after public comments and a report from this panel are received.

This review is a collaborative effort of the BPPD Insect Resistance Management Team which includes myself, Sharlene Matten and Alan Reynolds.

Today I will be presenting the information in a similar order that it is found in the written review.

First I will discuss pest biology and how it relates to Insect Resistance Management, dose, refuge, simulation models, monitoring for resistance, remedial action plan and also issues relating to grower adoption and education.

So, first I'll discuss pest biology. We have the western corn rootworm pictured on the left here and the northern corn rootworm pictured on the right.

There are aspects of both adult and larval pest biology that are very relevant when developing an insect resistance management plan, regarding adults aspects of mating and dispersal are very important.

Most information that we have thus far is on the western corn rootworm and there is also some limited information on the northern corn rootworm. And general -- for the western corn rootworm, females will mate within the field they emerge from with 20 to 48 hours after emergence.

So, they do not typically leave the field until after they have mated.

Prior to mating, these females may mover -- have been shown to move up to 10 rows within the field. However, mated females and un-mated and mated fit males can move between the fields.

There has been shown in general, there is limited dispersal of the corn rootworm adults. There is some evidence that there can be some long distance dispersals of the western corn root worm.

The northern corn rootworm movement is much more limited relative to the western corn rootworm and typically long distance movement is seen in the mated females. However, movement is typically good for the adults localized.

In addition to the movement and dispersal issues, emergence is important and research conducted thus far by Monsanto suggests that corn rootworm emerge from MON 863 corn 4 to 6 weeks later than from the non-Bt corn. This has relevance when deciding when and where to plant refuges.

Regarding larval movement, the larvae hatch as eggs in the soil -- from eggs in the soil and move towards growing roots. They are attracted to young growing roots probably from the carbon dioxide put off by these young roots and then they have been shown to move 12 to 6 inches in the soil, which relates to about 2 to 3 rows.

They are known to move from a younger -- from an older plant to a younger plant, they prefer this younger tissue. So, they may begin feeding on one plant and move to another, which also has relevance to where you place your refuge.

There is limited information regarding the movement of the western corn root, where most of the information we have is on westerns.

Although more information is still needed and particularly we need information on northern corn rootworm, Mexican corn rootworm and southern corn rootworm.

Monsanto has submitted some preliminary information on research underway regarding pre-mating adult dispersal, female flight characteristics, mating behavior, larval movement, larval feeding behavior and larval feeding behavior on MON 863.

However we still need a lot more information on movement, mating, emergence, patterns on Bt versus non-Bt crops. Feeding behavior which differs for the Bt crops and again, the other corn rootworm species.

We also know that the corn rootworm has adapted some strategies to current control practices that perhaps we can learn from when developing our IRM strategy for MON 863. This is a univalve pest with one generation per year.

It typically over-winters in the soil -- it lays its eggs in the soil and over-winters as eggs within the soil and emerges the following year and finds corn roots to feed on. The corn rootworm adults larvae do not prefer to feed on soybeans.

So, farmers have begun the cultural practice of rotating corn and soybeans. So, if the corn rootworm over posits in the corn the previous year, they will hopefully hatch on the soybean and not have anything to feed on and die.

The corn rootworm has now figured this out and they have adopted the strategy at laying their eggs at the end of the season in soybean, overwintering in these fields, so they can emerge the following year in corn fields.

In addition, the northern corn rootworm has adapted the strategy of extended diapause where it will lay its eggs in the cornfield, continue through diapause through the next growing season, when the soybean is growing and then emerge the following year in the corn plants.

In addition, there may be some lessons to be learned from previous resistance to insecticides. The corn rootworm has been shown to be adaptive resistance to organochlorines (ph), orthophosphates and carbamates.

However, this resistance was not detected until 10 to 20 years after the use of these insecticides.

Next I'll briefly discuss dose and how it relates to an IRM strategy.

A high dose has been defined by one of our FIFRA Scientific Advisory Panels as 25 times the dose required to kill all susceptible larvae. Although this definition was originally established for the European corn bore, we have adopted this definition thus far for the corn rootworm protected corn. We felt like it also applied here.

In a model developed by Caprio, moderate dose was defined as greater than 30 percent survival of susceptible larvae and a low dose was defined as more than 50 percent survival of susceptible larvae and at this time we have adapted these definitions of a moderate to low dose.

Research conducted so far by Monsanto has shown that 17 to 62 percent of the larvae will survive when feeding on MON 863 corn roots. So, this suggests we're dealing with a lower to moderate dose product here.

Dose can also be affected by the amount of the protein that will be ingested by the insect. In the case of corn rootworm, both the larvae and adults will feed on the corn plant so there is the potential of exposure at both life stages.

In addition, in the MON 863 corn roots, it has been shown that larvae do not actually feed and clip the roots, rather they graze along the outside of the roots typically on the growing region of the root tip and don't actually penetrate the roots. It is unclear if this is due to some sort of fitness cost or repellant property at this time.

Also a larvae may not get a complete dose throughout their life cycle because they may begin feeding on a younger plant and move to a -- as the plant ages, move to another younger plant -- from older plants to younger plants.

So, it may be moving from a non-Bt to a Bt plant or Bt to a non-Bt plant and may not be ingesting the protein throughout its larval development.

I have pictured here corn rootworm larvae feeding on corn roots. However, I wanted to point out this is not MON 863 corn roots, it was just to show larvae feeding on corn roots.

In addition, as I mentioned, adults will also feed on various parts of the plant. So, they may ingest some of the protein that way. It has been shown that western and northern corn rootworms will feed on silk's pollen and the ear tip. In addition, westerns will feed on leaves.

So, the dose they receive from these different parts of the plant will effect the dose they are getting throughout their lifetime.

Research conducted by Monsanto and submitted to the agency as part of their product characterization showed that the lowest level of Cry3Bb1 protein is expressed in the silks at 10 micrograms per gram and there is also some at low expression level and the roots.

Their product characterization showed an expression of 39 micrograms per gram. Another published study which looked at root expression assays showed expression of roots to be 58 parts per million.

Next, I will briefly discuss the three simulation models that Monsanto has cited in their development of their insect resistance management strategy.

All three of these models are based on the western corn rootworm only and they are also based on 100 percent adoption, meaning all growers are growing MON 863 corn, which particularly in the initial adoption is unlikely.

Models have been identified as important predictive tools in determining how to delay insect resistance. In particular, our 2000 FIFRA Scientific Advisory Panel identified the importance of using these models as predictive tools to develop an insect resistance management strategy, particularly prior to resistance actually occurring in the field.

These models can be used to predict possible resistance management strategies such as size and structure of the refuge. There are parameters of this that are -- that need to be input to these models that we need to have some background information on such as we need to know information on pest biology such as some of the aspects I discussed and also the initial resistance allele frequency which has not been identified yet for the corn rootworm.

So the three models that I mentioned that are cited in Monsanto's submission include a model developed by Caprio and modified by Monsanto.

Another model developed by Andow and

Olstad and an additional model that has been published by Olstad et al. and I'll briefly summarize these. A detailed description of these models is found in both the Monsanto submission and the Agency review.

First, I'll discuss Caprio's model. This was a model initially developed for the cotton bole worm, helicoverpa armigera in cotton and was modified by Monsanto to be adapted for the corn rootworm in MON 863 corn. This model appropriately considers insecticide application to refuges.

It is very likely and probable that growers will be applying refuge -- applying at least seed treatment or soil applied pesticides to their refuges.

This is two-patch model. This model considers pre-mating and post-mating movement to equal one. For post-mating movement, that is probably appropriate and also for male pre-mating movement, that is appropriate, but evidence has shown that the un-mated females or pre-mating females do not move out of the cornfield, so that may not be an appropriate parameter.

The resistance allele frequency was set at.0001 and although the official resistance allele frequency has not been determined for the corn rootworm, this is a standard for insects used in many models. This model also considers a 0 to 60 percent refuge.

Considering a 20 percent refuge as recommended in Monsanto's plan, this model showed that for a high-dose product resistance would be delayed for 19 years.

However, we're likely not dealing with a high-dose product when we discuss MON 863. For a moderate-dose product which was defined as greater than 30 percent survival of susceptible larvae with a 20 percent refuge resistance would be delayed for 11 years. With no refuge, this model showed that resistance would be delayed for eight years.

So, there is a 20 percent longer delay in resistance when a 20 percent refuge is planted than when no refuge is planted. For a low-dose product where more than 50 percent of the susceptible larvae survive, resistance is delayed for 17 years with a 20 percent refuge and 13 years with no refuge.

So, planting a 20 percent refuge would delay resistance 30 percent longer than planting no refuge at all according to this model.

However, we recognize that further validation and refinement of this model is needed. This model focuses on refuge size and not spatial parameters nor does it consider stochastic stimulation or spatial factors.

The next model that I will briefly summarize is the model by Andow and Olstad which is a deterministic model. It considers between field refuges. It also considers both continuous corn as well as corn rotated with soybean. It allows for the corn rootworms adaptation to be able to over-winter in soybeans as well as considering high risk areas with first-year corn.

A 5 to 50 percent refuge is considered.

However, it does not allow for the application of insecticides to the refuge acres. There were three different R allele frequencies considered in this model. Pre-mating dispersal was appropriately considered to be negligible. It allowed for random mating within fields and a high rate of post-mating dispersal which likely occurs.

This model allowed for five types of patches with the random post-mating dispersal as I mentioned.

In this model, a low dose was identified as 24 to 35 percent survival of susceptible larvae in the field with a low dose and 20 percent refuge. This model showed that resistance would probably be delayed for more than 15 years.

It also showed that resistance -- western corn rootworm resistance was not affected by over positing at the end of the season in soybean or corn. It showed virtually no difference between 100 percent continuous corn and the 40 percent continuous corn simulations in the number of generations needed for the R allele frequency to exceed .5. This model also needs further validation and refinement.

Finally, the Olstad model, which has been published, also considers continuous and rotated corn. It allows for two low -- two alleles -- resistances due two low and two alleles based on resistance due to crop rotation and resistance from transgenic corn.

It allows for the use of insecticides applied to the soil or seed treatments. Again, the resistance, -- the R allele frequency was set at .0001 and the time to resistance essentially was set at .03.

This model also appropriately accounted for the delayed emergence which may be happening of adult corn rootworm in MON 863 corn. It considers not just the block-type refuges but also the potential for row strips.

Genotype field and age are distinguished for adult males and un-mated females. Mated females are distinguished by genotype, field, age and genotype of mate. Corn phenology and aspects of pest biology such as adult dispersal, sexual activity, ovi position, sex ratio and survival of immature beetles is considered.

However, in this model they also consider re-mating of females and it is questionable the importance of this in the model since, according to the NCR 46, the bulk of the progeny will come from the first mating of females.

So, according to this model, if the resistance allele is dominant, resistance will likely occur quickly. It will show that 2 to 9 years -- resistance will be delayed 2 to 9 years as refuge size ranges from 5 to 30 percent for all high dose products.

If the resistance allele is recessive, resistance will take more than 99 years to occur. However, again we're not dealing with a high-dose product here.

This model also showed that row strips will lead to resistance quicker than planting the external block refuges.

In the lower-dose products, which is probably what we're dealing with with MON 863 corn, products with a 5 to 30 percent refuge planted as row strips delayed resistance, 2 to 6 years respectively and with blocks, 5 to 9 years, which shows that the row strips will delay resistance longer -- or I'm sorry, the external blocks -- I misstated, will delay resistance longer.

Again, I didn't mention that low doses defined by this model as greater than 20 percent survival of susceptible insects.

As I stated with all of these models, further refinement and validation is needed.

I'll briefly discuss the refuge size and structure.

Generally, requires a structured refuge be plant to delay resistance. A structured refuge will hopefully allow for susceptible insects to emerge so that they can potentially mate with the potentially resistant insects that may be occurring in the Bt corn rootworm protected fields.

Hopefully these insects would meet and their offspring would be susceptible to the Bt corn.

So, based on the information we have thus far, we have concluded that a 20 percent non-Bt corn refuge would be acceptable as long as it is planted with a similar hybrid to the Bt corn and identical agronomic practices are used on both the Bt and non-Bt acres.

Alternate hosts are not acceptable in the refuge acres. There is no evidence thus far that shows that they will produce enough susceptible insects to mate with the potentially resistant insects in the Bt field.

So, it must be non-Bt corn in the refuges. These refuges can be planted as blocks or in field row strips. However based on Olstad's model, blocks are preferred over rows even though there is some evidence -- for instance, the NCR 46 has recommended row strips over blocks. We concluded that blocks were probably based on the model delay resistance longer.

However, it is also acceptable to plant these infield strips as long as at least 6 to 2 roses are planted, 9 to 18 meters from the center of the Bt corn and again this is based on the Olstad model.

We recognize the need for growers to be able to treat their refuge acres with insecticides to control larval corn rootworm. So, seed treatments or soil insecticide applications would be acceptable in the refuge acres, however foliar applied insecticides for adult treatment would not.

Next, I'll discuss monitoring for resistance. Monitoring for resistance is important in determining shifts in resistance gene allele frequencies.

However, this requires baseline susceptibility data that we do not have thus far, although we are aware that this information is being researched and developed at this time.

There are other questions we still have

regarding a monitoring plan. For instance, the number of individuals needed to sample is unknown. There have been different speculations in the past regarding number of individuals.

One publication stated that if the phenotypic frequency of resistance is 1 in 1,000, then more than 3,000 individuals must be sampled to have a 95 percent probability of one resistant individual.

For the European corn bore and protected Bt corn, monitoring for resistance involves sampling at least 100 to 200 individuals per location.

Because of sampling limitations and monitoring technique sensitivity, resistance could develop to Bt toxins prior to it being easily detected in the field which is why it's very important to develop a very robust monitoring plan.

So, we recognize that more information is still needed for monitoring for resistance to MON 863 corn, a comprehensive monitoring plan that targets the corn rootworm and addresses when and where resistance will occur as needed -- monitoring for resistance is needed and should be developed within the first couple years of commercialization.

It is important to develop this as soon as possible because as more and more acres of the MON 863 corn are grown, monitoring will become more and more important.

In addition, we need baseline susceptibility data not just for the western corn rootworm, but also for northern corn rootworm, southern corn rootworm and also Mexican corn rootworm.

We need, as I mentioned, information on how many individuals for the corn rootworm should be sampled and how many locations and what areas should be targeted for this monitoring. Also resistant colonies need to be developed for comparative purposes and additional research.

Now, I'll briefly summarize the Remedial Action Plan.

The first step of remedial action is when suspected resistance occurs. Suspected resistance is essentially unexpected damage which Monsanto states should be reported to them by the growers. However, at this time unexpected damage for MON 863 has not really been defined.

We're dealing with a low-dose product so there will be some survival. In addition, it has been shown that the corn rootworm will actually graze around the outside of the corn roots as opposed to clipping the corn roots as in non- Bt corn.

So, we need to determine how will a grower be able to evaluate unexpected damage to report to Monsanto.

It has been suggested that this could possibly be done through root ratings. However, it is questionable that these 1 through 6 root rating scale currently used accounts for the grazing pattern of the corn rootworm, larvae feeding on MON 863 corn roots.

In addition to -- once the unexpected

damage has been reported to Montana, then in vitro and in planta assays would be needed to be conducted to confirm that the plant is actually expressing the Cry3Bb1 protein, because it could be they are surviving because it's just not MON 863 corn.

To confirm that this suspected resistance is actually resistance occurring, susceptibility levels should be compared to baseline levels. This could be done preferably by a discriminating dose assay, but also looking at neonate progeny.

Just to show, this is what the 1 through 6 root rating scale looks like. In a typical non-Bt corn, somewhere around 2.5 is where economic damage is considered to be occurring.

In addition, I mentioned neonate larvae could be used to compared to baseline levels to determine if resistance is occurring. That would essentially be comparing the LC 50 in a standard diet bioassay of the suspected resistant individuals to the baseline levels that should be developed.

It has also been stated that susceptibility could be determined from neonate larvae if over 50 percent of the root nodes are destroyed under controlled laboratory conditions.

So, once suspected resistance has been confirmed to actually be resistance occurring, this should be reported to EPA within 30 days and mitigation measures should also be reported to the Agency and undertaken within 90 days.

These mitigation measures should involve immediately informing growers and extension specialists and other interested parties in the area resistance is occurring.

Sales should be ceased in that area immediately and should not reassume until consultation with the EPA. Alternate control measures for corn rootworm should occur and be recommend to extension specialists, seed dealers and growers and intensive IRM measures should be implemented as soon as possible.

In addition to the planted structured

refuge, there will be initial anticipated low grower adoption and hybrid availability, which I will discuss now.

Monsanto anticipates there will be initial low adoption rate for various reasons. First of all, they anticipate it will take awhile for information to be disseminated to all growers, seed dealers, extension agents etcetera.

Growers will need time to evaluate this technology, see how it is working for their neighbors. In addition, other control measures are in the pipeline such as additional seed treatments and potentially other corn rootworm resistant corn. So, you don't anticipate there to be this 100 percent adoption of MON 863 corn.

It has been shown from surveys that growers will typically plant more than one hybrid. So it is not anticipated that their whole fields would be MON 863 corn.

Also, basing assumption on experience with previously registered, generically engineered corn and soybeans where they have shown generally in the first year there is less than 5 percent adoption, less than 20 percent in the second year and less than 40 to 45 percent in the third year.

However, the agency recognizes there is no guarantee that there will be this low adoption rate by the growers. In fact, we have seen publications that have speculated that adoption of this corn rootworm protected corn will be much quicker than the already registered transgenic crops.

Monsanto also speculates that the availability of the hybrid will be limited initially due to breeding and manufacturing limitations.

In their submission they suggest that less than 50 percent of the market share of seed companies will be distributing MON 863 corn and they stated that they need at least four to five years for all of their hybrids to be available as MON 863.

I will now briefly discuss grower education, which is very important to resistant management. It is actually the growers that will be implementing these IRM strategies.

So, it's very important that we get a simple comprehensive word out to them that -- and that they get all the current information. This can happen through technology use guides, Internet sites, 1-800 numbers, stewardship training courses. Surveys have shown that growers get most of their information from their seed dealers.

So, it is important to train these seed dealers of insect resistance management strategy so they can pass the information onto growers. We need to work with relevant work groups such as the USDA, Extension Agents, the Northern Corn Growers Association -- the National Corn Growers Association -- I'm sorry.

It is important to continue grower surveys to make sure that the growers are getting the appropriate information and implementing the appropriate IRM plan.

As I mentioned, it is important to get a consistent message to growers to alleviate confusion, keep it simple.

We also at the Agency believe it is important for these technology use guide to be signed annually, so that as information evolves and potential new strategies evolve or change, the most current information is getting to growers and we know that they are reading it as they sign the technology use guides each year.

We strongly believe that education will lead to compliance if the growers know what to do, they'll do it.

So, in conclusion, we do not anticipate -- we believe that a 20 percent refuge that is planted as infield row strips or preferably adjacent blocks will be adequate to ensure that resistance will not occur from the corn rootworm to the Cry3Bb1 protein at for at least 3 years.

And we recognize that all these acres should be treated agronomically similar and that refuges may be planted -- may be treated with insecticides to control corn rootworm larvae.

We believe that more information needs

to be gathered and should happen during the initial three years of commercialization of this product.

A lot of this information is already being gathered. We need much more information on pest biology for the western corn rootworm and especially for northern corn rootworm, Mexican corn rootworm and the southern corn rootworm.

The models that have been developed so far need refinement and validation. A comprehensive monitoring for resistance plan that targets the corn rootworm and MON 863 corn is needed.

We need definitions of suspected and confirmed resistance that are adequate for MON 863, appropriate mitigation measures and grower education is very important for the insect resistance management strategy.

I wanted to point out that we are only talking about insect resistance management for MON 863 corn rootworm protected corn. We recognize that stacked products are on their way, but a separate insect resistance management review and strategy would have to be considered for stacked products.

Thank you. I thank you especially -- the -- our Chair and the panel for giving me this opportunity to present all this information this morning.

DR. PORTIER: Thank you very much Ms. Rose.

Any questions from the panel?

DR. PORTIER: Dr. Caprio.

DR. CAPRIO: Robyn, you mentioned that there was delay of 4 to 6 weeks coming off of corn?

Is that correct or is it 10 days?

MS. ROSE: The information I recall from the Monsanto research and also in the NCR 46 position statement to us was that it was delayed 4 to 6 weeks.

DR. PORTIER: Any other questions from the panel?

DR. NEAL: I would like to make one

clarification --

DR. PORTIER: Dr. Neal.

DR. NEAL: -- with mating of the western corn rootworm, you had a slide that showed most of the mating occurred between 24 and 48 hours and a lot of the mating occurs within the first hour of emergence. So, it should really be 0 to 48 hours.

MS. ROSE: Thank you.

DR. HUBBARD: One point of correction. Everything in the document here is 10 days instead of 4 to 6 weeks. In my own personal experience is that it is 10 days delay.

DR. GOULD: Was your conclusion there was no pre-mating male dispersal or I didn't --

MS. ROSE: Just no pre-mating female. We do anticipate that males will disperse prior to mating and --

DR. GOULD: When you were commenting on the models, it sounded like you were saying it was appropriate to assume no pre-mating dispersal, but just for the females?

MS. ROSE: Just for the females, yes.

Thank you.

DR. PORTIER: Dr. Andow.

DR. ANDOW: You gave dose expression levels. I believe those are reasonably constant for a certain period of time. Could you elaborate on when they start to drop?

MS. ROSE: Unfortunately, no I can't. That would come more under our product characterization. I don't know if John -- we can get that and perhaps see if we have that information or see if Monsanto has it.

DR. ANDOW: I just wanted, again, to compliment you on your concise presentation of a lot of information.

DR. PORTIER: Any other questions?

It is 9:35 and we're a little bit ahead of schedule. I think we'll go ahead and start with the public comments and take public comments until around 10 o'clock and then go on break.

Dr. Storer from Dow AgroSciences. Is Dr. Storer here?

For the public commentators, if you

could come up, identify yourself, who you are speaking on behalf of and go through your presentation. I believe all of you have agreed to a 5-minute presentation time unless other agreed to with EPA that I don't know about.

And after your comment, we'll let the panel ask any questions of you.

DR. STORER: I requested 15-minutes if that is okay?

DR. PORTIER: Paul is not here, but go ahead, 15 minutes is fine.

DR. STORER: I need the overhead projector.

DR. PORTIER: Do we have an overhead?

DR. STORER: Thank you.

Sorry for the technical difficulties getting started.

My name is Nick Storer, I'm with Dow AgroSciences by way of background. I received my Ph.D. in Entomology from North Carolina State University.

The science behind IRM and specifically, I developed simulation model of post adaptation to Bt corn and Bt cotton. At AgroSciences, I am responsible for insect resistance management over all insect resistant traits.

I am also Chair of the IRM Technical Subcommittee of the Agricultural Biotechnology Stewardship Technical Committee or ABSTC. This is an industry group that coordinates responsible stewardship of Bt corn among the various registrants.

The building of my Ph.D. work -- I have developed a model to help understand the durability of rootworm resistant PIPs to aide sciences and stewardship of our product development.

The model lends itself pretty well to other rootworm traits such as MON 863. So, I believe my model can help the panel address some of the questions that the Agency is asking of them today.

I appreciate the encouragement I received from various members of academia industry and the government in development of this of this model and I appreciate the opportunity to share it with the panel this morning.

Starting with the key questions, my model can address -- and I think it's of relevance to the panel today. The first question here is kind of a catch all. "What are the properties of the insect biology population and farm operations and the rootworm resistance traits themselves that affect the durability of these traits?"

And Robyn this morning has gone over some of this information as has been presented to them by Monsanto.

How do dose and refuge size affect predictions of durability? How does market penetration affect predictions of durability and how does having a mosaic of alternatives rootworm resistance traits affect predictions of durability of each of those? These are the areas I'm going to address this morning.

This is spatially explicit stochastic simulation model for these rootworm traits. In developing the model, I tried to incorporate as much of -- as is know about the pest biology, the crops -- how the crops are used and the agricultural environment in which they are going to be used.

The model tracks insect populations and genetics in each of the fields in a region under assumptions that I can vary -- parameter values I can vary and deployment scenarios that I can vary.

So, we can examine the effects of some of these different properties on how durable the trait is likely to be. So we at Dow AgroSciences are using the model to devise long-term plans to protect the durability of our rootworm resistance traits. But as I say here, it's -- I've modified it to compare it with the more moderate dose trait that Robyn presented data on this morning -- is indicated for MON 863. I believe this approach is complimentary to do that of the other models as -- the other models that Robyn presented this morning. This is an example of a region that I'm modeling.

In two years -- so this is a grid of fields and then the color of the field, the color of the square indicates what crop is growing in that field. So, we have a mixture of conventional maze, the rootworm resistant maze and soybean.

In this situation, I have a strict rotation between maze and soybeans. On the left in year one is maze and on the right in year two is soybean and vice versa.

What I'm looking at is how do the insects -- the population biology of the insects within these fields and then how do they disperse among those fields.

I won't read all this in detail. The panel will have access to these slides for their deliberations. As I said, trying to account for as much of the pest biology as possible. Some of the important aspects here are -- depend on lava mortality.

Random mating within fields, then among fields, females mating only once, fecundity and survival through time.

No immigration. So, I'm assuming that the area represented by my model is also representative of all the areas around that model. There is no influx of insects that have been exposed to a different selection regime.

One of the key aspects I think Robyn was pretty clear about this morning is how do the adults disperse. So, I wanted to try and over that quickly.

Ten adults in the model do not fly, that is, those that is those that within 48 hours of exclusion -- once they do disperse, the probability of leaving the field they are in depends on the phenology of the crop that they are in.

So, more mature now, the more life that will be dispersed than if the field is in flower, for instance. Then, where they go to is based on the distance from the source to the destination field.

Also the relative attractiveness of the

fields in the area. So in the graph on the right -- this is the probability of flying to each of the fields in a region from the center field. You can see the greatest probability is that they actually remain in the field that they are trying to leave.

So, this is some kind of trivial dispersal with the field, but then also they can move out to neighboring fields, up to two fields away. And then the probabilities of those depends on the distance and the relative attractiveness, which depends on the phenology of the crop in those fields.

So, with the default parameter settings that I am going to present today, all females mate in the field that they emerge from. They are not necessarily by males from that field, male dispersal pre-mating does occur and there is 30 percent of the ovi position on average is in the natal field.

The remaining 70 percent is distributed around the region according to this kind of probability distribution.

So, the agroecosystem (ph) I want to present here -- I'm trying to simplify it a little bit. I'm just going to look at continuous corn. This will probably be the area where adoption of this technology is growing most rapid.

I'm allowing for insecticides to be used on the non-rootworm resistant corn such as the refuge, but I'm going to assume the farmers are following the IPM recommendations, so their decisions to treat or not treat will be based on the pervious year's adult population.

Finally, the distribution of resistant and nonresistant corn fields is re-randomized each year for these simulations.

The final assumptions are around the genetics of adaptation. Some of these assumptions are probably the most important aspects that need to be considered.

Firstly, for lack of anything -- any information -- lets assume the resistance is going to be controlled by a single gene with R or S alleles. This is the most high-risk case where just one gene is involved.

Assume that gene is not sex-linked and assume there is no fitness loss associated with that gene, I'm assuming zero mutation. They have an initial frequency of the R allele of .001. This is the higher end of the spectrum that people usually use as an initial frequency.

Finally, the functional dominance for the resistance gene depends on dose. Functional dominance is probably one of the most important parameters so, I want to spend a little time describing how that relationship is established for this model.

Here we have a plot of dose mortality response. The black line is for susceptible insects so the theoretical line that you can read off from a dose here of measuring it relative to the LC 99 allele scale.

So, at a relative dose of 1.0, you've got 99 percent mortality of susceptible insects. Of that same dose have you around 80 percent mortality of the heterozygote insects.

If you go down to a lower dose, say 1/10th of that, then you have around 90 percent mortality of susceptible insects and less than 50 percent mortality of susceptible insects.

This is assuming that heterozygotes in this case are 25 times resistant to the trait -- Resistant ratio of 25. There is no reason to necessarily expect that, except that's the value that previous SAPs have come up with for defining high dose. So, I thought, I might as well use that right now.

Then you plug in the numbers for the mortality or the fitness of those two insect genotypes to come up with a calculation of the functional dominance value, which ranges from 0 to 1. Then you can plot what is the functional dominance or age against the mortality of susceptible insects.

You can see how as mortality declines from 100 percent, you expect the functional dominance to increase from being recessive to essentially being dominant. The precise shape of this curve is going to depend on all the assumptions from the previous page, particularly, the level of the resistance ratio for heterozygotes.

If it is less than 25, the slope of this curve will be somewhat shallower, but it will still follow the same path and the dose and functional dominance relate in this time and manner.

The output from this model, I measure the relative rate of adaptation. Though the model measures the increase in gene frequency through time, the true rate of this increase is kind of unpredictable because the population dynamics of the insect are unpredictable.

We don't know from year-to-year what size the population is likely to be. We also don't know a whole lot about the genetics I've already alluded to. We don't know a whole lot about grow behavior.

There is a lot of uncertainties in the

model, so what we can do instead, rather than predicting time to certain gene frequency, just compare how that rate of increase changes with different parameter settings and different deployment scenarios. So, I come up with a relative rate of adaptation, where I compare any given simulation with a benchmark. For the benchmarks, I use a functional dominance of 0.1 on a 20 percent refuge. I get my relative rate of 1.

If the model predicts a relative rate of 2, for instance, it means adaptation would occur twice as fast or in about half the time of the benchmark, everything else being equal.

So, that's the output that I'm going to be presenting to you today is going to be expressed in these terms.

So, we can look at what is the effect of dose as measured here by more mortality of susceptible insects as I did on the previous slide on the relative rate of adaptation.

So, here on the extreme right-hand side

you can see as you approach very high doses where mortality is close to 1, the model predicts the relative rate of adaptation is going to be lot slower than for doses that are 95 percent or less mortality of susceptible insects.

So, for instance, if you look at the 50 percent mortality, the 0.5 mortality, that's an adaptation rate of around -- relatively around -- adaptation rate of around 2. Compare that with relative rate of adaptation around .1 for those higher doses. So, the model would suggest that those higher doses would promote durability for about 20 times as long than that lower extreme.

So, you can take a couple of those points that previous slide assumed 20 percent refuge is planted. You can take a couple of those different doses and look at different refuge sizes for those two.

So, I think that what essentially has been previously defined as high dose with 9.99 percent susceptible mortality -- so, this is pretty much recessive resistance low heterozygote survival.

Compare that with a lower dose here, 90 percent susceptible mortality. This gives a more codominant level of functional dominance.

So, you can see very quickly that to obtain the same level of durability with a high dose, say durability of around 1, you need a much lower -- a much higher refuge for a more moderate dose.

Also look at just the slopes of those curves indicates to me that the refuge size doesn't help a -- a small refuge size doesn't help a lot in promoting the durability of a more moderate dose product as it does for a high-dose product.

I think one of the corner stones of the interim plan that Monsanto has presented the Agency is that not all farmers will plant the crop initially for the first few years. So, I use the model to simulate the more patchy distribution of rootworm resistance maze. So, in this case, on the left, we have a picture of the region again, where some areas are still rotating between soybean and maze to control the rootworm.

Other areas are adopting the rootworm resistant lines and planting at 20 percent refuge. Then on the right, we can look at how does the percentage of the different management techniques affect the durability of the rootworm resistance trait.

So, for 100 percent on the extreme right of the graph, the adaptation rate is going to be greatest in the lower end of the spectrum adaptation rate is going to be lowest.

This slide also highlights again, 20 percent refuge doesn't make a whole lot of difference especially at low levels of adoption. At the high levels, it does extend durability maybe twofold -- one and a half to twofold at the low end. It's really not making much difference.

The slope of these lines is a lot steeper for the higher dose product. This is -- for these runs, I wanted to show you what it does for the more moderate dose that I have been discussing so far.

Finally, I wanted to address what happens when there is more than one trait available to the growers. I'm here thinking about the products that AgroSciences has in the pipe line. I believe there are others as well.

So, the rootworm is going to be faced with a more complex scenario than just choice between refuge and transgenic. They are going to be exposed to different toxins out there. So, you can look at how does the -- how does that affect the durability of the product.

Here we have type 1 corn, which is the more moderate dose. And then type 2, which is a higher dose. It's actually my default assumptions. You can look at -- you can see how the rate of adaptation to the more moderate dose declines as the percentage of maze planted to that dose, to that trait, declines as you move from right to left. That's the blue line. Similar effects as you move from left to right with the gray line for the type 2, the higher dose.

The higher dose gains more by the plantings of the lower dose, because the lower dose is producing a significant number of susceptible insects, whereas the reverse is less true.

So, that's what I want to present to the panel today. Hopefully, it will be of use in your consideration of suitability of the Monsanto's proposed IRM plan.

DR. PORTIER: Thank you Dr. Storer.

Are there any questions from the panel?

Dr. Gould.

DR. GOULD: When are you looking at those last two slides, are you looking at gene frequency in the entire region or in the areas where the adoption occurs?

DR. STORER: I calculate gene frequency taking over the population over the entire region.

DR. GOULD: So, if it's -- do you have any insight into how bumpy that is in the regions of adoption?

DR. STORER: Yes. Certainly, in the region of incomplete adoption, the slide previous to this where we had areas where the soybean was being rotated with maze in some areas. You get a very steep gradients between areas where they are using the transgenic and the areas where they are using the soybean.

DR. GOULD: I just want to follow-up, because you -- this presentation is very important for the panel.

You are always looking at relative rates of adaptation in the different schemes. One question that comes up in terms of the partial adoption is that are you looking at rates of adaptation in that early period.

I guess my question is how does the early, partial adoption impact rates of adaptation after greater adoption?

So, when have you these bumpy sort of landscapes in terms of allele frequency, do you have any sort of insights into how that has an impact? That's important for our deliberations.

DR. STORER: When measuring just the rate of increase in the gene frequency, it doesn't really depend much on what the gene frequency is. So, I think, until you get certainly, up to gene frequencies around .1, the effect is fairly small.

So, the rates of increase in gene frequency, if it starts off as a low frequency or after a few years is at a low frequency in a given area, it is going to be the same rate as if it had already been selected.

DR. GOULD: That's, I guess, my question about those regions where it is intensely used within small regions if that gets you over that gene frequency in those regions.

DR. STORER: That depends on where you start.

DR. GOULD: Okay. And just one final question.

You do use this relative adaptation -- rate of adaptation compared to your default. We do want to be able to compare your model to the others in some way. My sense of the way you wrote that, the default is a rate of adaptation of about.32 or something? So, basically as it goes from the initial frequency of .001 to .1 in three years?

DR. STORER: I would have to work back through that calculation.

DR. GOULD: It would be good if you could give the panel that information, because to compare to it the other models it would be useful. I understand your reasons for not wanting to give number of years. But that's my calculations on that.

DR. PORTIER: If I could follow up. I had a question along the same lines, I guess.

You have run every situation of the model here with greater than 90 percent susceptible non-survival or susceptible death, and yet the presentation we just had said it is about 20 to 62 percent mortality -- I mean, survival -- larval survival, which is clearly not in the range of 90 percent mortality. What is the impact of that?

As a follow up, you have put the resistant allele frequency at .00 -- 1.001 -- was that percent or .001 real.

DR. STORER: .001, real.

DR. PORTIER: So, .1 percent.

And yet with such a low mortality in these populations, how do you know that the resistant allele is not at a much higher frequency of as much as 20 percent?

DR. STORER: Let me address the second question first.

We don't know what the initial gene frequency is. I haven't seen any measures of that. The assumption of initial gene frequency is usually based on an assumption that there is some kind of a fitness cost and that there has been no prior selection for that. So, really there is a balance between mutations and the fitness cost that establishes that initial gene frequency.

Mutation rates in insects have been

measured but not in this particular insect to be in the order of 10 to minus 5, 10 to minus 6.

So, if you assume that that mutation is going on but there is also some kind of fitness cost, you end up with a balance that usually ends up the gene if it's not being selected for in any manner being rare.

This survival of the crop right now, I'm assuming that there are insects that don't carry resistant genes, they are just the more tolerant end of the spectrum in the dose mortality response for susceptible genotype -- gene by environment interaction etcetera that allows survival.

To address the first question, most of the runs I ran were not less than 90 percent mortality. I guess, that's because -- you know, it came from the slide of this model that the Dow AgroSciences brought it to mind where we're certain we have much higher levels of mortality than that.

I did have that one slide which showed mortality down to 50 percent. It showed that the rate of adaptation starts to decline somewhat slowly below 90 percent, but eventually -- obviously, if you get down to zero percent mortality then the rate of adaptation is zero. At some point, that curve has to drop off more steeply but it hasn't dropped off more steeply by 50 percent mortality.

DR. PORTIER: But would it -- that was -- I wanted to follow up on that curve specifically. Would it drop more rapidly if the resistant allele frequency that you started with, instead of.1 percent was say, 2 percent or 10 percent? Would it drop much more rapidly in that 50 percent area?

DR. STORER: I would have to think about that, that's not something I have looked at.

DR. PORTIER: Any other questions from the panel?

Dr. Andow.

DR. ANDOW: I'm sure you mentioned this and I just -- it just -- I just missed it in terms of exactly how is this rate defined again?

DR. STORER: The equation for this rate is that gene frequency after X years divided by the initial gene frequency, the natural log of that, the whole thing divided by that X years.

DR. ANDOW: Gene frequency -- is that a weighted average of the population -- that's all fields --

DR. STORER: That's the gene frequency taken across all insects in the population. So, yes. It is average -- it is NOT --I'm not weighting it by -- it's weighted by the population size in each field, but I take all adults, add them up together.

DR. ANDOW: Thank you.

DR. PORTIER: Any other questions from the panel?

Dr. Neal.

DR. NEAL: Yes. Can we go back to the curve where you have the mortality versus -- relative to 99 percent versus log dose? And to generate that particular curve, is that based on actual LD 50 testing of rootworms?

A No; it is not based on LD 50 testing of rootworms with Cry3Bb, since I don't have access to Cry3Bb.

So it is a hypothetical curve. I think I stressed that at the time.

DR. NEAL: Okay. When I looked at that curve, it seemed to me to be unreasonably flat, that it should be much steeper than it is. I'm wondering what effect steeper mortality versus log dose curve would give.

DR. STORER: I use a slope of 1 for that line.

Obviously the steeper that line, the lower the heterozygote will be at any given dose. Though the next line on this curve would be somewhat flattened.

If you could imagine the next curve that I'm thinking of, the functional dominance dose.

DR. PORTIER: Dr. Hubbard.

DR. HUBBARD: I just wanted to get -- compare your model to the history and the biology of this insect. We know that resistance has evolved to crop rotation. We know that resistance has evolved to adult sprays, insecticide sprays.

We know that resistance has evolved to broadcast use of insecticides. Those insecticides have long residual times. Each of these may classify as high dose, yet you state that high dose promotes durability.

Soil insecticides have anywhere from 27 to even more adults -- 27 percent of the susceptible population compared to untreated check. Sometimes there are even more adults produced from soil insecticides.

So, you may classify that as a low dose and so you are stating that high dose promotes durability whereas the history of this insect -- that isn't necessarily the case. I'm just looking for your comments.

DR. STORER: I think with the current applications of soil insecticide, there is a large portion of the population that escapes treatment.

So, they are not being selected for resistance. So, that looks more like infield refuge as opposed to a low dose. For those -- the broadcast cyclodienes, for instance, resistance of those in about a 10 year time frame probably is when they first started seeing resistance.

I've run simulations of that through my model, looking at what is known about functional dominance resistance to that class of insecticides in insects in general. It appears that it is not recessive and a high dose assumes it is going to be recessive. That's kind of what those functional bell curves were aimed at.

So, it looks as though that didn't fit the pattern of high dose because hydrozygotes survival was probably rather higher than I'm implying here. That's why it evolved more quickly.

DR. PORTIER: Dr. Whalon.

DR. WHALON: This is more of a general question.

I noted that you -- one of the assumptions you made was continuous corn. I just wondered if you back up a little bit and looked at alternative sources, mortality-like rotation, like sea treatments, like adulticides, what would you anticipate from your functional dominance at that --

DR. STORER: I think if you have a -- have insecticide treatment to the transgenic field and not to the refuge field, you would end up increasing the durability of the Cry3Bb in a rotated scenario.

It is hard to see how the farmer is likely to use the transgenome in first-year corn unless he has problems with rotation resistance that Robyn described this morning.

In that situation, I found ways to use the transgenic crop to actually manage that and bring down the frequency of that rotation resistance by having a small refuge that is continuous corn and not transgenic. It kind of acts as a refuge for both and then if you plant your transgenic onto the first-year corn, essentially you are going to kill off all those rotated -- rotation resistant insects.

Does that answer your question?

DR. WHALON: Well, that helps. I'm just thinking in terms of more realistic situations, particularly where there are other modes of action out there and what that would do. I think a model like you presented would be really useful to look at that as well.

DR. STORER: The slide that is up there now kind of addresses that, where there are two options for treatment. They don't necessarily have to be transgenic options they can be -- what I'm calling here, type 2, could be an insecticidal treatment.

I haven't looked too much at adulticides. This is all larval mortality in the model. It certainly could be adapted for that kind of study, too.

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: Dr. Storer, have you ever used your model to look at the amount of refuge versus what you might expect with sort of like population suppression and interaction of population suppression and refuge sizes?

DR. STORER: Can you explain a little more what you're thinking?

DR. HELLMICH: Well, like I'm thinking that if you have a smaller refuge, there is going to be fewer insects that are going to be produced and therefore growers may be less likely to spray in some of the refuge and how that might factor in.

DR. STORER: That is actually built into the model as I presented it today, with the farmers using IPM to decide whether or not to treat the refuge.

So, if the region-wide population the previous year is low, then the probability that they will use an insecticide on the refuge is low. I don't see the opposite applies.

Where we have high levels of use -- it's only the higher doses that I based my modeling with -- population suppression is quite dramatic. So, there is a -- less of the refuge gets treated.

I have also run the model where the

refuge is always treated that didn't make a whole lot of difference. If the refuge is never treated, you get some extension of durability.

DR. PORTIER: Dr. Gould.

DR. GOULD: I just want to follow-up. A number of the panel members have had access to your paper. It's a very important paper and I think it would be very useful if everyone on the committee here had access to it. Is that possible?

DR. STORER: Yes. I don't see a problem with that.

DR. GOULD: Your question, specifically, I think some of the simulations you have done -- people have been asking you is in the paper and it could be valuable to us.

DR. STORER: Right. I need to stress that paper. I really was looking more -- the way we're working with than what we are looking at today.

DR. GOULD: But it could be made available to everyone?

DR. STORER: Yes. Probably not today, though.

DR. GOULD: It could be shared among us?

DR. STORER: Oh, absolutely, yes.

DR. PORTIER: Any other questions for clarification?

Dr. Andow.

DR. ANDOW: Correct me if I'm wrong, but if the rate -- that rate ratio is 2, then that means that the time to resistance is half?

DR. STORER: That's correct.

DR. ANDOW: Okay. So -- you know, the difference between 1 and 2 is actually substantial.

DR. STORER: Right.

That is on a log scale because it's the difference between 1 and 10 is the same as the difference between 1 and .1.

DR. PORTIER: Dr. Storer, thank you very much.

We're going now take a break for 15 minutes. My clock says it is 12 after 10, so we'll start again at 10 30 promptly.

DR. PORTIER: Dr. Andersen, did you have any comments on the previous discussion or any questions?

DR. ANDERSEN: No I don't. I think there was one question we were trying to find a little bit more information on and I think Robyn has been able to get more some more information only on the distribution overtime of the amount of protein in the tissues. I think she is going to share it. We'll get some copies made and share it with them.

DR. PORTIER: Thank you very much.

Dr. Rissler, welcome. Please introduce yourself.

DR. RISSLER: Good morning and thank you for the opportunity to comment today. I'm Jane Rissler with the Union of Concerned Scientists, a nonprofit partnership of scientists and citizens working for sustainable solutions to environmental problems.

I work within UCS's food and know

environment program where we advocate for a transformation of US agriculture to a profitable, productive, sustainable system that is healthy for people and the environment, while ensuring that citizens have a say in how their food is grown.

To the SAP members here, we very much appreciate all the time and effort that service on there panels requires. It's an important public service.

To EPA, both the staff here and elsewhere, we are grateful for the decision to devote considerable resources in money and staff time and effort to hold three days of meetings. It is no small undertaking.

Some members of this panel served also on the committee that produced the recent National Research Counsel report on USDA's regulation of transgenic crops. As they and most of you know, USDA's oversight suffers from it's failure to seek outside, scientific advice. FDA oversight shares this same deficiency.

However, we recognize that EPA efforts

to again expert advice in public settings from the scientific community are in stark contrast to the other two agencies.

We applaud the Agency and we are encouraging USDA to look at EPA's use of the SAP as a model for increasing the scientific rigor of its reviews.

Members of this committee have the comments which we, along with Environmental Defense submitted to EPA in late May, on the proposed registration of MON 863.

Drs. Charles Benbrook and Angelika Hilbeck provided analysis upon which these comments were based.

We recommended that EPA turn down Monsanto's request to register MON 863 because the company has failed to demonstrate the absence of unreasonable risks as required under FIFRA.

The company also failed to provide a strong, credible insect resistance management plan. Moreover, we concluded that the benefits of MON 863 may be modest due to its marginal efficacy and the declining use of high-risk chemical insecticides for corn rootworm.

MON 863 benefits may also be short lived because of the inadequate resistance management.

As you know -- as you well know, the proven ability of corn rootworms to adapt underscores the need for effective IRM plan for MON 863.

However, because it has not developed the information needed today, design of a strong, long-term plan for MON 863, Monsanto is proposing an interim approach.

The temporary plan, though improved in some respects over earlier Bt crop plans, has a number of serious flaws. Monsanto has not developed the data or modeling needed for an effective IRM plan. To design one, whose long-term goal is to prevent or very significantly delay resistance to MON 863, Monsanto must develop a substantial body of biological, behavioral and genetic data and simulation modeling.

That body of information, as the morning's discussion made quite clear, does not yet exist. Critical information, as you heard this morning, is lacking in a number of areas. For example, on the dispersal of adult corn rootworm feeding behavior of larvae, effective dose of MON 863 and corn rootworm genetics.

Modeling projects to help predict the emergence of resistance under various managing strategies are underway again as you heard this morning, but they are not sufficiently developed to make the needed contributions to IRM plans.

Speaking as a person who knows very little about this modeling area, the results this morning further confused my ability to figure out what ought to be done under this interim plan.

So, to avoid delay in marketing MON 863, while gathering the data that it should have, Monsanto has proposed this interim plan. Now the interim plan itself, while it has some improvements over other plans, it too is seriously flawed.

For example, its shortcomings include its dependence on the marketplace to dictate refuges, an inadequate 20 percent grower established refuge, an incorrect definition of resistance, inadequate requirements for treating refuges, doubtful assumptions about the impacts of MON 863 on continuous corn acreage, lack of modeling results that address the use of insecticides on refuges, lack of clear connections between grower education efforts and the implementation of the IRM plan, failure to address resistance issues associated with northern corn rootworm and inadequately developed monitoring and mitigation plans.

As a result of these inadequacies, we have recommended that the Agency defer registration, pending the development of a strong creditable plan.

However, given the very high likely hood that EPA will approve Monsanto's request for registration, we have urged the Agency to impose several restrictions, including limiting registration to one year to allow incorporation of new information readily, restricting planting to no more than 25 percent of corn acreage in a county, requiring larger refuges and requiring the company to submit results of modeling and statistically valid research to fill the significant gaps that have prevented it from developing an effective long term plan.

Thank you.

DR. PORTIER: Thank you very much. Thank you Dr. Rissler.

Are there any questions from the panel?

Thank you again.

Our next public commentator will be Mr. Gary Queen.

DR. PORTIER: Welcome Mr. Queen. Please identify yourself and who you are speaking on behalf of.

MR. QUEEN: Good morning. I'm Gary Queen, from Burlington, Colorado. I'm representing Queen Farms. I've been farming for about 20 years north of Burlington, a farm about

5,000 acres.

I have a brief, opening statement and several points I would like to make.

Corn rootworm work is single most significant insect that growers like me must contend with. Every year we have to treat for corn rootworm, costing roughly $18 per acre.

Sometimes we must also use a rescue treatment when our first treatment does not work, costing an additional $10 to $14 an acre.

My first point is on safety. It's very important to us. With the protection against insect damage built into the seed, growers are not exposed to dangerous chemicals and pesticides and rescue treatments are very dangerous to use and to the wildlife in our area.

I would like to be around to see my grand kids and this technology makes this one step closer by eliminating more chemicals in our environment.

Simplicity. With an ANC solution, growers will have a more simple approach to insect control than ever before. Using this convenience, growers will be able to utilize their time at planting more efficiently.

Effectiveness. Rootworm protected corn is more effective than any other treatment -- any other traditional pesticide treatment. Insect control is not compromised by factors like weather conditions that can affect soil and foliar applied treatments, providing more consistent insect control.

By being able to use this technology, it will open up more avenues for us to use as far as irrigation. We have a severe drought in our area and we are running out of water. We have the opportunity to use drip-aid, which is 100 percent efficient in watering. We can use this now with new technology to save our water and to grow a better crop with rootworm tolerant corn.

Growers want to have access for the long term. We also know the realities of least resistance development as we all see in the important chemicals lose effectiveness because of resistance and we don't want to -- and we want to make sure that we are able to use this for years to come.

Then most important, it seems like anymore -- the money factor. We will be able to make more money by using this technology by eliminating crop losses due to crop consultants not being able to see the pest on time.

Time considerations. There is a narrow planting window and planting delays can impact yield. Using this technology will help us speed up the planting giving us a better opportunity to maximize our yields. We need to have a flexible IRM so that we can have a 20 percent refuge be on adjacent fields, so we can cover more acres while planting.

I use a 16 year-old planter and it would slow the planting process up tremendously if we had to clean out the planter on every circle to plant conventional corn for the refuge.

I plant one number for the entire circle, thus eliminating the chance we will have a planting problem on that field. We have multiple pivots, so we could easily use one for the refuge. I just want to emphasize that flexibility is the key and we're not going to use a product that will slow down the planting process.

New technologies are not the problem. We are concerned with yield drag and we will slowly use this into our system. We hope to use about 10 percent a year to see how the yields are. And to give you an idea, on my farm with this technology, we have seen great results.

Thank you for your time.

DR. PORTIER: Thank you, Mr. Queen.

Questions? Dr. Hellmich.

DR. HELLMICH: Mr. Queen, where did say you were from? I missed that.

MR. QUEEN: Burlington, Colorado.

DR. HELLMICH: Burlington, Colorado.

Okay. I want to thank you for coming, because my experience in the past is that the growers are the cornerstone for any kind of insect resistance management program and I thank you for taking the time to come here to present this information.

Also, I have a question for you.

As an entomologist, I was humbled a few years ago to learn that insects are very low on the priority list of -- at least some growers, when they come to thinking about their crops. They are more concerned about the seed and the herbicides and everything else.

Do you think that given the European corn bore resistant management plans and in the advent of this product that growers are becoming more aware of resistance management and will be willing to be good stewards of this product?

MR. QUEEN: I'll give you one example. We used to have a chemical called "Glean," that we used in our area. We are not able to use that anymore because of resistance buildup to weeds and so everybody learned basically, after that we need to have a good refuge and not to lose this because it is going to save us money in the long run, definitely.

DR. PORTIER: Dr. Gould?

DR. GOULD: I was just wondering, how many acres do you have within one pivot -- when you were talking about that?

MR. QUEEN: One pivot is an average of 120 acres.

DR. PORTIER: Dr. Whalon.

DR. WHALON: I too, commend you for coming and presenting your thoughts. I think they resonate with some of us Applied Entomologists.

The question I have for you, I would like to you explain to the panel how you make rootworm control decisions now.

MR. QUEEN: Basically, what we do for our rootworm control is we put down insecticides at planting time. Right now we are using Regent. We have used previous chemicals in the past like Counter and then if we have to do a rescue treatment, we have to come in with Furadan, and I just hate Furadan. No odor in that. You can't tell it has been sprayed on.

So, if you have a problem out there

and are you not thinking about what happened two days ago you go and work on a system, you got it -- who knows how long it will shorten your life.

DR. WHALON: Do you use the corn rootworm rating system in the fall to make decisions?

MR. QUEEN: The one to six, yes.

DR. WHALON: Who does that in your operation -- it's a large operation?

MR. QUEEN: I have a crop consultant that comes in and evaluates my fields once a week.

DR. WHALON: Thank you.

DR. PORTIER: Any other questions from the panel?

Thank you, Mr. Queen.

MR. QUEEN: Thank you.

DR. PORTIER: Ms. Helen Inman.

Welcome, Ms. Inman.

MS. INMAN: Thank you very much, Mr. Chairman.

I have previously visited with Mr. Lewis and asked to have a extra minutes, if that's permissible and also, I have brought some written testimony along with my oral comments. So, I would appreciate if this could be distributed to the panel.

Thank you.

Good morning. My name is Helen inman. I am a corn soybean farmer from North Central Iowa. I farm with my husband Ross. We have been farming for 44 years. So, we have been in the business for a long time.

Ever since biotech became available to us, we have planted both corn Bt and herbicide resistant soybeans.

This morning, I would to like to offer some comments in support of MON 863.

I currently am the Vice Chairman of the NCGA Biotech Working Group and I also am on the Iowa Biotech Committee and I am a past Chairman of the Iowa Corn Promotion Board.

I would like to tell you just a little bit about NCGA. NCGA represents 48 member states with over 32,000 and we get funding from over

300,000 producers. Most of our funding comes from farmers.

NCGA represents farmer interests in many different areas, including biotechnology and farm policy.

As a producer in an ever changing world, I'm very much aware of the effect of biotechnology on our industry and I am a big biotech supporter.

Currently, in our farming operation, 100 percent of our soybeans are herbicide resistant and from -- anywhere from 55 to 60 percent of our corn is a Bt corn. We make our planting decisions based on economics, safety, and marketability. And we often do plant herbicide resistant corns, depending upon whether we can channel our corn to other markets.

In my 45 years of farming, I have noticed a lot of changes in the industry. We have currently are enjoying higher -- much higher yields but our tillage practices have also changed. We have gone from the old moldboard method of tillage to minimum tillage and even no till. But with that has come a greater dependence upon pesticides.

Biotechnology can help us cut that pesticide use. I currently volunteer on both NCGA and the Iowa Biotech Committees, because I am convinced that biotechnology is needed in our world.

I'm here today to tell you some of the growers's perspective on this new technology. I think that the farmers that I represent through NCGA would want you to make decisions based on sound science. My operation and all of our operations are based on flexibility. We need IRM rules that are going to be workable and consistent.

If the IRM regulations are not workable, it will be much harder to implement them. And the burden of the implementation is going to be on our shoulders.

Thanks to biotechnology, the farmer leaves a much lighter foot print on our environment. In our own operation, we no longer spray for corn bores. And with our herbicide resistant soybeans, we are able to get by normally with one application.

We use a non-residual herbicide and so we do got have any problems with getting into our groundwater. In addition, we can reduce our tillage and slow our soil erosion.

Corn rootworm just as other controls, takes dollars. Corn rootworms take a lot of yield away from farmers. It costs between $15 and $20 an acre to treat corn rootworm. But it is important too, even though we're going to have reduced pesticide use, that we are able to use pesticides when and if we need to.

This brings me to the need for a farmer-friendly, consistent, science-based IRM regulation program.

I think that the National Corn Growers, seed companies and universities would all agree that we need to have responsible stewardship of biotechnology and we as farmers definitely do agree on that.

We have spent many hours, a lot of checked off dollars in educating ourselves on IRM practices. Our commitment is strong.

To preserve the many benefits of biotechnology, it is necessary to implement a good IRM program for corn rootworm technology. And I think that growers realize that if they are not willing to implement this practice on their own farms, they do run the risk of losing access to the technology.

Improper use of this technology will, of course, shorten the life span of the technology.

During the planting season, as one of my predecessors pointed out to you, we're faced with a lot of unplanned issues. We're trying to get a crop in the ground, weather can offset some of our decisions, maybe we can't get a certain hybrid. These issues come up real quickly and if we have too complicated an IRM program, we will not be as able to implement this program.

In order for IRM regulations to be widely accepted by farmers, we need to have a farmer-friendly regulation. Sometimes what works in modeling isn't going to work on the farm.

Like all US Regulatory decisions, IRM regulations for corn rootworm must be based on sound science. I think farmers probably will comply if they can -- point it out to them that there has been good research done on the regulations.

We encourage the use of NCR 46 group to determine sound science for resistance. But we understand that science is changing rapidly and adjustments may be need to be made as these products -- as new products come on the market.

As farmers, we're well aware that agricultural biotechnology is important for producing good quality, safe foods and fiber. But more so, it is also important for conserving our vital assets of land and water.

In the past, the EPA has relied quite heavily on NCGA for their expertise in developing programs and implementing those programs and NCGA encourages EPA to continue this relationship.

As with the corn bore technology, NCGA will encourage our producers to implement IRM plans when planting the corn rootworm corn. This is an EPA requirement and we know that it is the right thing to do to preserve the technology.

In conclusion, I would like to leave this thought with you. I want to leave as light a footprint on the environment as I can do. And to do that, I feel that I need to maintain the technology.

This technology, though, needs to be farmer-friendly. It needs to be consistent and flexible and above all, it needs to be science based.

Thank you very much for your time.

DR. PORTIER: Thank you Ms. Inman.

Are there any questions from the panel?

Dr. Hellmich.

DR. HELLMICH: Ms. Inman, as a fellow Iowan, I would like to welcome you to the committee and thank you for coming all this distance to give this presentation.

I would like to say that I an appreciate the National Corn Growers Association input in the past with NS 205 Committee and Bt corn.

I would like to point out that they were very instrumental in helping to -- to have the input into that and recognizing the importance of that. I know they have a web site where they talk about resistance management. I hope that that will continue with this product.

MS. INMAN: We're definitely planning on that.

DR. HELLMICH: Thank you.

DR. PORTIER: Dr. Wise.

DR. WEISS: Ms. Inman, thank you for coming today.

I would like to ask a question following up on Dr. Whalon's question of Mr. Queen.

How do you currently make your rootworm management decisions on your farm?

MS. INMAN: Well, as I pointed out, we do have a corn soybean rotation. When we do need to use corn rootworm, protection, we do a soil-based application.

But we don't have to do it -- we personally do not have to do it all the time. We are getting some growers that are going to a corn-corn- soybean rotation -- corn-corn-corn-soybean rotation and they are really interested in this technology.

DR. WEISS: Following up on that, do you have a crop consultant or do you base your corn rootworm decisions based on sampling?

MS. INMAN: We do have a -- we use an elevator consultant for that.

DR. WEISS: And Bancroft, Iowa -- help me with my geography -- is that in Northwest Iowa?

MS. INMAN: No. It is in North Central, Iowa. We're actually about 30 miles from the Minnesota boarder. I think we're kind of up there in God's country.

DR. WEISS: I'm from Minnesota. I would agree with that, although you're about 30 miles short of actual God's country.

Do you have problems in that area with northern corn rootworm extended?

MS. INMAN: Yes, we are. We don't have real extensive yet and personally, we haven't noticed a whole lot, but I am getting -- having comments made to me by some of my farmer friend that they are seeing a lot of that.

DR. WEISS: Okay. Thank you.

DR. PORTIER: Dr. Andow.

DR. ANDOW: So I'll continue with the Minnesota connection. I'm a Minnesota also -- University of Minnesota.

MS. INMAN: Good. We like Minnesota.

DR. ANDOW: Great place to be.

I have a couple questions about decision making and drawing on your experience.

In terms of -- you said you used a lot of the corn bore product, the Bt corn -- the corn bore.

MS. INMAN: Yes.

DR. ANDOW: I know in those areas of Minnesota at least, there is a lot of -- a reasonable amount of use of that product, I'm wondering, when the room product comes on, it is not going to be associated with the corn bore product.

What kind of trade-offs do you see people are going to make in terms of deciding whether or not to plant the corn bore product or the corn rootworm product -- because they are not going be able to plant one variety that has both?

MS. INMAN: Well, at the present time, probably not, but I think it is going to be -- in my own case, and I can only probably talk from my own experience, I would have to really -- as we adopt the technology, we probably would go into it very carefully. We're not just going to jump in and plant all rootworm technology and maybe not even as quickly, because we don't have quite the need that we did for the corn bore.

So we will we would ease into it. And probably -- we have some individual fields, some smaller individual fields.

So, perhaps I would envision that we

might try it on that as opposed to the other. And if it was far enough away -- that wouldn't work, would it? But that's the way that I would envision we would approach it.

DR. ANDOW: And your neighbor that are doing the corn-corn-corn-soybean rotation, do you think they would be more willing to go into the corn rootworm variety? What is your feeling about that?

MS. INMAN: They probably adapt a little quicker than we will because they are going to be seeing more problems than we do currently today.

DR. ANDOW: I would like your opinion about -- if there was some IRM plan that was implemented today, but say three years from now it was changed, how do you think growers would respond to that?

MS. INMAN: Well, I think that growers -- so long as it could be kept pretty consistent with what the plans are for -- like say corn bore, I think they would be comfortable with it and I think that they would adapt to it.

I know we're going to have to look at this on an event-by-event, because you know, different events are going to be -- I'm not a scientist, but different events are going to require -- might require -- but the more consistency we can have, the better off we personally will be, but also, the better chance of compliance there will be.

DR. ANDOW: Thank you.

DR. PORTIER: Dr. Hubbard.

DR. HUBBARD: On behalf of the Corn Growers Association, I was hoping you may speak to the number of acres that are treated or planted to herbicide resistant corn. You mentioned you planted herbicide resistant soybeans. I was curious on that.

You may or may not be aware corn rootworm larvae can develop on a number of grassy weeds that are present in corn fields. The product being talked about today is not as affective with larger insect larvae and may not be as compatible with herbicide resistant corn. I was curious if you have a knowledge on the amount of acres of --

MS. INMAN: I'm sorry, this is not -- not being a scientist, I can't answer that question.

DR. HUBBARD: Well, the question, just basically just has -- how much corn is planted with herbicide resistance traits?

MS. INMAN: Approximately, about 30 percent of the acres are planted to a -- that corn.

DR. HUBBARD: Is that sprayed at what phenology of corn is it -- the corn out of the ground or does anybody -- you may not be aware of it, but --

MS. INMAN: I know that there is, but I'm sorry, I can't tell you the -- because I unfortunately, do not do the spraying on my farm.

DR. PORTIER: Any other questions from the panel?

Dr. Neal.

DR. NEAL: Yes. Ms. Inman, thank you

very much for coming.

I was wondering if you could comment on the logistics of what a grower would need to do to put in-row furrows in as part of an insect resistant plan versus planting a separate block.

MS. INMAN: I'm sorry. I'm not sure that I understand your question.

DR. NEAL: Part of the plan that is being discussed is to plant a refuge of corn as a set of rows within a field for the corn rootworm as opposed to the corn bore insecticide resistant plan where adjacent blocks are allowed.

MS. INMAN: Well, actually, even in the corn bore plan, you can intersperse and as a matter of fact we are. It just so happens in one of our fields that that works real well. And a matter or logistics -- part of it would be the kind -- the type of planter you have.

If you have a planter with a lot of boxes, that's not real hard to do. Or you can go ahead and clean your planter, if you have a large drum. I wouldn't be as handy, but when have you a series of boxes, it is perfectly -- it is done.

At least it is done in my area where we can have non Bt -- non corn bore resistant corn right along side with a corn bore resistant corn. So that can be done. It is being done for corn bore technology.

And I think the same thing could be done for the rootworm.

DR. NEAL: In terms of being farmer-friendly, would it have any logistical problems in adding an in-furrow insecticide treatment to the non transgenic corn and not treating the transgenic or would that be something that be something that a grower would tend to do or would you just leave off with the insecticide treatment?

MS. INMAN: Well, I think that -- it can be done, it definitely could be done. Of course, part of the it would depend on whether you still had the insecticide boxes on. But it definitely can be done and it would need to be done. I think they would if they had to.

DR. NEAL: One further question.

Would you anticipate using a transgenic product on your first-year corn for corn rootworm or corn coming in after your soybean rotation?

A I guess that's going to depend partly on the number -- as this particular rootworm continues to appear in our area, because it is spreading. It is just begin to go come in, probably not as much as I would on second or third year.

DR. NEAL: Thank you.

DR. PORTIER: Any other questions from the panel?

Thank you very much, Ms. Inman.

MS. INMAN: Thank you for the opportunity.

DR. PORTIER: Mr. John Beshaler.

If I pronounced your name wrong, I apologize.

MR. BESHALER: Good morning. That was fairly close. My mom pronounces it Beshaler and dad pronounces Beshaler, so you can pick anything you want.

I am a farmer from Central Nebraska. I deal with commercial crops. I raise corn, wheat, soybeans, alfalfa. These are sold to local elevators and to local feed lots. And I just wanted to take this opportunity to address panel today and give a viewpoint of the farmers's perspective.

When I make planting decisions, I look at three things, efficiency -- how easy is it. Economy -- does it put money in my pocket. Environmental issues -- is it healthy, is it good for my farm, am I being X posed to chemicals, are my hired men being exposed to chemicals, so on and so forth.

Efficiency -- looking at this rootworm corn, what I do is put corn in the hopper and plant. I just fill it up and go. I don't have to worry about bags of insecticides. I don't have to worry about plugging problems in the insecticide hoppers. I don't have to worry about application problems, equipment problems, and so on and so forth. I just, like I say, just fill the hoppers up with seed and go plant.

Economy-wise, the injury is still out there. I haven't harvested this corn. It will be harvested in about a month and a half or so. I'm looking at some healthy plants, that's one thing that I can see. The agronomy of things look fairly decent.

That's probably how it would pay for itself if it did pay for itself. The technology fees that the farmer will have to pay Monsanto will be offset basically, by savings in insecticide payments. So, there probably won't be much of a savings there.

The environmental issues -- we're looking at not exposing ourselves to insecticides. And the way I planted my corn I do what they call a T-band where I just basically, spread a band of insecticide at planting time on top of the ground.

Some of it gets down into the furrow, but I just leave it on top of the ground. And anything that comes across that can get into it.

And it does. And you know, you just -- it is not insect specific and it just -- let's face it.

If we were here and had this corn rootworm for years, and we're here trying to justify this new technology of insecticides, I would be laughed out of this room. We probably wouldn't even be here. I think we're kind of heading in the right direction in that respect.

So anyway, rootworm corn I think is -- I think from a farmers's standpoint is giving us everything that I'm looking for -- Ease of planting, economy -- who knows, maybe that will be all right. The environment seems to be -- seems to be there. We're trying to figure that out today.

I'm not seeing any dead birds. I'm seeing plenty of insects in this particular field. So far it looks good.

Just to comment on the IRM. That's a big issue today. Talking about 20 percent refuge either within the field or adjacent to, from a farmers's standpoint, that's doable.

Also, to the rescue treatments that need to be done from time to time coming back in and over spraying for different insects. I understand this to be either you can spray the whole thing or nothing at all. And that is also doable.

So it looks to me like it is a win-win situation and that's why I'm here to help relay what I'm seeing as a farmer.

DR. PORTIER: Thank you Mr. Beshaler.

Are there any questions from the panel?

Dr. Federici.

DR. FEDERICI: You mentioned you already have some experience with this technology. Are you speaking of corn bore corn or --

MR. BESHALER: Oh, I might have misspoken -- rootworm. I planted 100 acres this year and so I got a chance to look at that -- one hundred acres through this growing season. Yes; I'm sorry -- of corn rootworm -- rootworm, yes. Did I say, corn bore?

DR. FEDERICI: No. No. I was just --

MR. BESHALER: Because rootworm --

there's rootworm corn. I planted 100 acres of it on a particular field of mine and so, I got a chance to look at it.

DR. FEDERICI: Your assessment is that it is working as anticipated.

MR. BESHALER: My assessment is we have a draught out there and it's testing things and it is looking healthy -- let's put it that way.

I have not done a yield check on it, so, in my mind, the jury is still out on whether or not it is going to pay for itself.

DR. PORTIER: Dr. Weiss.

DR. WEISS: Thank you for coming.

I would like to follow up on a question I asked a the previous speaker, Ms. Inman, what kind of crop consulting -- or do you use a crop consulting basis?

MR. BESHALER: I have a crop consultant that comes in once a week. The way we handle rootworm is to apply the insecticide at planting time. The way we know which fields to treat is by beetle counts during the summer so we will not treat anything that doesn't need to be treated, in other words.

DR. WEISS: A follow up on Brian's question, you haven't dug any roots yet and taken any --

MR. BESHALER: My agronomist has not done that. He's a pioneer man and he did say that things look healthy. We have no lodging. Monsanto people have come out.

I have gotten a little piece of paper from them that they took root ratings. On this particular field, the insecticide worked and the different friends between rootworm corn and insecticide corn was about even there wasn't much difference.

We had a little test plot there with no insecticide, conventional corn. I would estimate 25 percent yield loss. I mean, just like night and day there. Root lodging and a lot will depend on the weather coming in when we harvest.

DR. WEISS: This is irrigated corn?

MR. BESHALER: This is irrigated corn

and draught conditions and we just weren't able to keep up this year with the irrigation, but yes, it is under a pivot.

DR. PORTIER: Dr. Federici then Dr. Whalon.

DR. FEDERICI: Do you know what the soil insecticide is applied or did your consultant do it or do you know?

MR. BESHALER: We applied force. I can't tell you if that is organophosphate. You guys would probably know that.

DR. PORTIER: Dr. Whalon.

DR. WHALON: I would just like to follow-up on this rescue treatment and what you do now and -- not in the corn rootworm corn but in your other corn, how often -- what is the frequency that you have to come in and do something after have you treated, say, made a decision to treat a field in the summer or fall and then you treat -- seed treatment in the spring when you plant, how often do you have to go back in and do something remedial?

MR. BESHALER: Not very often. This year we had spider mite problems. That was the first time I have had to do anything for 10 years with spider mites. So, that was a treatment we came back in.

The corn bore problem -- we used a -- we are very heavily corn-on-corn in our area and the corn bore problem was always a problem, especially in certain fields. But ever since the corn bore corn came out, we just haven't had any problem there.

So, we have not sprayed for, I would say five years for corn bore. So, we have sprayed one time in five years.

DR. WHALON: Because economic drives a lot about your decisions about what hybrid to take and whether or not this technology has application for you.

Do you have any handle on if you had to put a rescue spray on more frequently in this type of approach because an insecticide in the soil at planting as broad spectrum kills more than one species.

MR. BESHALER: I don't think it would be a problem. At planting time we have wire worms, maggots, things like that that you would not have to come back in and spray. Corn bore -- rootworm -- we do have beetles. I have never sprayed for beetles, but people do in our area. And that would be the rescue treatment we would be talking about. If the beetle count got too high and started clipping silk and all that. But I have never had to do it; I have never done it. I have had enough control, I guess, from the insecticide application that I've never done it.

DR. WHALON: Some of the concerns that I've heard is that maybe growers are going to have to come in and control wire worms and maggots and things like that in time. Of course, no one knows at this juncture, but it's a possibility which might take away some of that economic insensitivity to move, since are you using a broad spectrum now.

I would like follow up on that, for you

to just address, maybe how you feel about handling treated seeds and things like that or application -- band application at planting with conventional insecticides right now and how does that playoff against the transgenic corn coming down the line?

MR. BESHALER: Well, this rootworm corn coming down the line, the corn I got anyway had seed treated insecticide called Goucho. I would not touch with that with my bare hands. I'd wear mask and gloves.

So, you are dealing with an insecticide that is designed to cover those insects out there other than rootworm.

So, that I think is going to be the standard. I can't say that. I'm not speaking for Monsanto, but I would say that has to be part of the treatment, that there has to be something out there that covers that or else it is not going work. We have more than corn rootworm out there and we have to cover those type of insects.

But the fact that you don't have to handle insecticide in another bag there, it would be worth something to the farmer.

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: Ms. Inman before suggested that this new product -- she would ease into it, just try a little bit of at a time.

I guess my question for you is, is that what your plan is? What do you think most growers will be -- over this three-year horizon, what do you think growers will be doing at three years from now?

MR. BESHALER: Well, I'm thinking that if this thing gets on the market, I'm thinking it is enough of a no-brainer, where we don't have to mess with insecticides, then I'm thinking it will be used heavily.

What was the first part of your question?

DR. HELLMICH: How you would ease into it within three years?

MR. BESHALER: I wouldn't use it unless I had to. I would not buy that technology unless I had to. The only reason I would do it is if I had high beetle counts and that's -- and I would be a typical farmer in that respect. I would take a beetle count and if I had to use it, I would use it.

It would be a situation where it would be applied to a corn-on-corn rotation or just corn-on-corn, no rotation about it.

That takes in -- in my area, that's a lot of the irrigated acres, which amounts to about 25 percent of the acres and it wouldn't be something that would be economic feasible on dry land corn, because we do have rotations and it just probably wouldn't be applied there in my area.

DR. HELLMICH: So, you would still use a crop consultant and determine, based on his recommendations whether to even plant the corn?

MR. BESHALER: Yes; that's what I would do. Take that beetle count -- that's his job.

DR. HELLMICH: In a pivot situation, how do you think that growers are going to approach that?

MR. BESHALER: That's a good question. In my case, I would not want to alternate rows. In other words, apply soil insecticide in one or two rows and nothing in the other one except the rootworm corn. I wouldn't want to do that myself. That's something that we're allowed to do and probably would work good. I don't see a farmer doing that.

I see farmers planting blocks of land, maybe half a pivot or a full pivot and having the refuge beside it. In other words, plant the planter load full of rootworm corn, get that done, go to the next project -- putting insecticide in your planters and do it conventionally for the refuge.

Do it all at once without doing half a planter one way and half a planter the other way. That's what I foresee.

DR. HELLMICH: So, partial pivots may be the solution in this case?

MR. BESHALER: Yes. Yes. That would be --

DR. HELLMICH: Is that practical for most growers?

MR. BESHALER: Yes. Yes we can do it. A lot of guys they don't like to -- you know, they don't like to clean out their planters anymore often than they have to, naturally.

But a lot of guys will plant a planter-load for instance -- it might be 40 acres and then they can switch over.

You know, you have you such a small window of planting opportunity and they want it to be as easy as possible. But this new technology is important. We have got to be good stewards and I'm hoping we can do it as farmers.

When what I foresee is that there has to be some way to go back in and oversee this thing. Whether the seed companies do that or somebody, because there will be abuses. You know that.

There will be times when things aren't done properly. And I think there has to be some type of regulation there some way that's easy and palatable to the farmer and to the seed companies and that sort of thing.

DR. HELLMICH: What kind of oversight would you suggest?

MR. BESHALER: That's a good question there. EPA wouldn't want to come out to the farm and be the tough guy, but there really needs to be some way of verifying some of these things that we don't want any abuses. We don't want these things to get resistant any faster than they have to.

I actually think it is going to be a natural thing in my situation. I'm only going to treat the fields that have to be treated. That's only going to be probably 10 percent of my farm.

For me, it is going to be very natural. It is not going to be painful or anything like that. The farmers in our area will be in the same boat.

DR. WHALON: I would just like to rejoin on a thing that you said earlier. I think I just need to understand it better. That is, you got from Monsanto this year in that one hundred acres you planted in that rootworm corn, Goucho treated seed?

MR. BESHALER: Yes. That's what I understand. They treated that seed with Goucho. They had not only the rootworm gene in there, but Goucho.

DR. WHALON: Thanks.

DR. PORTIER: Dr. Hubbard.

DR. HUBBARD: My question has to do grower behavior.

According to Monsanto, 50 percent of the current available market will not have opportunities to plant transgenic Bt corn for rootworm .

How likely is it that somebody is going to switch from pioneer, for instance, to rootworm resistant corn?

MR. BESHALER: I think it is going to be economical. There is people out there, myself included, that get along quite well with Pioneer. We're going to look at how good that particular variety does in that particular area.

This corn rootworm will be a tool that

we use, but the main thing will be the yield that we get out of those fields.

DR. PORTIER: Dr. Gould.

DR. GOULD: I just want to follow up on Marks's question to you about this Goucho treatment. So, the Goucho is along with the Bt corn?

MR. BESHALER: I think they just mixed it in there, yes.

DR. GOULD: And it was also used in the non BT?

MR. BESHALER: No. No. the non Bt was not even a Monsanto product, as a matter of fact. It was just a conventional corn with a seed -- or a soil applied insecticide, with a test strip where we had no insecticide.

DR. GOULD: And the test strip did not have Goucho?

MR. BESHALER: Right. That was on that conventional hybrid.

DR. PORTIER: Thank you very much, Mr. Beshaler.

MR. BESHALER: Thank you.

DR. PORTIER: Jon Tollefson.

Welcome back, Dr. Tollefson. Please identify yourself.

DR. TOLLEFSON: I'm Jon, Professor of Entomology from Iowa State University. Following those comments from the Minnesotans about land north of us, I grew up in Minnesota as well. When I grew up they told me I should move south where the winters are nicer, so I did. I now reside in Iowa.

But I began working with corn rootworms in 1967 and I have studied corn rootworms continually since that time with the exception of about three years when I was offered a federal job with the military that I couldn't turn down. So I joined the faculty in 1975 at Iowa State University.

I have been -- essentially, my research has involved management of corn rootworms. I have specialized in the areas of sampling, decision making and, if you will Applied Ecology of the corn rootworm.

I'm going to do two things today. First of all, you have I think been given the written comments from NCR 46, the technical committee -- regional technical committee on the corn rootworm.

I'm going to take this opportunity to fill in some background on how those comments came about in being composed and submitted and then I'm going to go forward from that and speak as a scientist from Iowa State University and not representing NCR 46.

In 2001, I was the Chair of the NCR 46 technical committee, in January, in which we discussed the preparation of a written statement concerning Monsanto's initial IRM plan that had been submitted to the Environmental Protection Agency.

NCR 46 did that and submitted that letter on May 30th or May 31st of 2001. That is the seven-page document you have in which we addressed issues concerning IRM for corn rootworms in general and in some cases we went specifically into the Monsanto Yield Guide Registration Application.

In the following year, essentially, that -- let me back up. That letter was signed by the executive committee of the NCR 46 Committee, the Executive Committee of NCR 46 consists of the Secretary, the Chair -- I left the Chair -- and the past Chair.

And those people signed the letter for the NCR 46 Committee after the NCR 46 Committee voting members had reviewed the document and wordsmithed the document so that it reflected the unanimous opinions of the NCR 46 Technical Committee.

Last year at that same time, we went through the process of rather meticulously identifying and confirming voting membership on the NCR 46 Committee. And we also have participants in the meetings. So basically, that first draft was agreed to unanimously by the voting members of the NCR 46 Committee and signed by the Executive Committee.

At our 2002 meeting in this past year, we moved to -- because of the continued concerns in IRM, we went to a structure in which we created a subcommittee to deal with IRM. This was a subcommittee of the NCR 46 Technical Committee.

That subcommittee consists and is chaired by Lance Mickey (ph) from the University of Nebraska. It includes Ken Osley (ph) from University of Minnesota, myself at Iowa State University, Elson Shields (ph) from Cornell University and existential members are the chair and chair-elect of the NCR 46 Committee that was being -- Christy DeFonzo (ph) and Mark Martell (ph) respectively with a liaison with the University -- or Canada, which would be Arch Shasma (ph), because of their interest in our registration.

The second written document that came out this year from NCR 46, again was circulated to the voting members of the NCR 46 Committee for agreement on the content and it was signed off by the IRM Subcommittee.

In that second document, it reaffirmed that May 31, 2001 support for conditional registration of the MON 863 event.

The logic for asking or endorsing, I guess, or supporting would be a better word, the conditional registration, although it appears likely that during the interim registration that resistance would develop due to the reasons you have heard already.

Low dose of expression -- probably there would be survivor-ship on it. The initial marketing penetration would probably be limited.

Third current models simulated on low dose with limited penetration predicated and low probability of resistance.

Fourth, resistance appears evolve in local levels, so the key to IRM, even during an initial product launch is to prevent excessive repetitive use of the technology at the individual farm level.

I'm quoting from the second document but

I want to emphasize personally, the comment on repetitive use of the technology at the individual farm level, because one of the questions I think that was raised by the EPA document that has been put together as a summary is, if there are restrictions on planning of the MON 863 technology, at what scale should this restriction be? Should it be on a regional scale, a state scale, a county scale?

I'll come back to that when I have gone into my personal scientific comments.

And then the EPA also has stated that in the NCR 46 Committee supported the idea that conditional registration is needed so that we can do some of the research projects that are necessary to gain the information that will allow us to make sure that we have a robust IRM plan.

Finally, a conditional IRM plan, registration, would allow the consumer, the farmers, to get experience and have an opportunity to evaluate the MON 863 technology and the application of the IRM plan.

Now I'm going move away from the NCR 46 position statements and I'm going to speak as an entomologist from Iowa State University. I'll come back to that issue that I introduced.

That's the scale of a restriction on the planting of MON 863. It's my personal opinion that we're talking about macro-scales and micro-scales. I was involved in the modeling activity at Iowa State University.

And in that model, they calculated that rootworm insecticides sides were not necessary because across the country there is enough corn and soybean rotated that you could rotate all acres and it wouldn't be necessary to use insecticides.

That is a macro scale model, dealing with natural corn production. When you look at individual farmers, individual farming practices differ based on a number of reasons, whether it is the soil types and production practices.

And you are and you are likely to see much more pockets of very intensive corn MON culture. So, mon counsel tour. So, even though the initial release would be less than what would supply the market, there is a possibility that there could be local foresight where the yield guard MON 863 technology could be extensively planted an applied selection pressure.

There is a question concerning the monitoring of the -- for the further development of resistance and the suggestion that Monsanto has proposed, that growers would use the root rating scale for excessive root injury.

It would be my experience -- well, first of all, the grading scale that EPA provided this morning was the 1 to 6 Iowa State University rating scale. The rating scale now that we're using is the no injury scale, which is O to 3 scale.

More importantly, it is much more intuitive for the grower to learn that the 1 to 6 scale. I have been teaching that through my extension responsibilities for the last couple of summers and the growers catch on very easily and to the 0 to 3 no injury scale, because it is very intuitive.

It would be much easier for them to use. It's also much more sensitive at lower levels of root injury you would likely see with a genetically engineered variety.

Having said that, I think it is unlikely that growers would be able to detect the early stages of resistance developing, based on root ratings.

It is rather difficult to get a representative sample of roots from the field, clean them off properly and actually distinguish the difference between rootworm larval grazing on the surface of the roots and other abnormalities based on cultivation trimming or growing in rocks and so forth.

One thing I could possibly suggest if the panel would consider something like set no fields where you could use a delayed planting like in trap groups to draw beetles in and then run a lab greenhouse bioassay on beetles collected from a region.

That's only a preliminary thought and I would have to think more about that as far as the gene flow basically, of what you are pulling into that trap crop.

With remediation and corn rootworms, we have some possibilities yet include will crop rotation and insecticides that would allow us to do some things if resistance would appear to be happening. There were some comments made in EPA presentation this morning. One had to do with dispersal and movement by the insect. It indicated that the -- I think Ms. Rose indicated that the adult male would move between fields.

My experience is that I'm a little bit more conservative on my estimate of the movement between fields. A Purdue study that was done, I think by Godfrey and Turpin (ph), indicated that when they had corn following soybeans that it didn't have a resident population of rootworms, the predominate sex that cam into that field was the females. It's about an 85 percent female population that comes into that field.

When we have flown beetles in the past we get our dispersal activity predominantly in the female. Our flying of males has been cursory and it's being done more intensively now, to see if the males will actually disperse distances.

Coats (ph) and Tollefson found that about 15 percent of the females will do this - dispersal -- that Ms. Rose referred to. So, if you want a figure on what the long range dispersal probability is on females, we get about a 15 percent level.

In an unpublished dissertation Bruss (ph) reports that about -- that the trivial movement within a field of rootworms is about 17 to 18 meters per day.

If you are talking about a 24- or 48-hour pre-mating period for females, that would be basically a distance that we would estimate that would be possible for beetles to move trivially within a same field.

There was a comment this morning that --

and this is where I'm going get into some dangerous ground, David, about the onset model and that a block planting of a refuge was better than a strip planting of a refuge as far as durability in a resistance management plan.

The only thing I would ask is that, does the model assume that with the block planting in the same location have you increased population of susceptible rootworms developing in that field and because they are breeding in that field they are more successful in the population builds.

If that's case, I would suggest there is a carrying capacity that is going to be reached in that blocked planing. At a point are you going to get to a level of diminishing returns in which the population will become ostotic to a sustainable level that can be maintained by the biomass of the field.

I'm in dangerous ground because I do not understand what assumptions were made in the model, so I say that -- make that comment with caution.

There is also a suggestion that resistant colonies be developed so that lab and greenhouse bioassays can be conducted with corn rootworms. The reason we have more information on the western corn rootworm than the other species it has been the one that has been more successfully reared than, for example the northern.

The northern has been almost impossible to rear in numbers great enough to do laboratory research which means that if you get into lab bioassays and extended diapause, northern corn rootworm species, it is going to be very difficult to do that take out.

One of the questions asked of was growers was the likelihood of treating the refuge ground.

One of the things in my experience with growers in Iowa when this happened, when you got into areas of heavy rotation, is that there was an advantage with the hopper box planters as opposed to one large box -- a movement to a larger seed box for greater seed capacity.

If you go to a three-bushel seed box as opposed to a two-bushel, you sacrifice the insecticide boxes to make room for that, which means to go to a transgenic corn and extended diapause and then have to treat the refuge, means you still have to go through a modification in which you would go back to a smaller seed box or go to a plumbing for a liquid application like Regent or Furinol (ph) and post emergence or seed treatment.

And finally, I would -- my experience would suggest probably that the growers are more likely to embrace the corn rootworm transgenic technology more quickly than the European corn bore technology that came out with leps (ph).

I say that because in Iowa there were infrequent applications made for European corn bore control prior to the release of the transgenic corn and when the transgenic corn was released, people started to see an advantage to managing corn rootworm.

And the embracing of the corn bore technology increase escalated after that observation. With the corn rootworm, when corn is planted after corn, though farmers will routinely use a rootworm control action -- they will use soil insecticide for example -- and these soil insecticides decisions are often made in advance and a prophylactic control is used, like a spring application of a band treatment or post emergence broadcast application. The seed technology in a --

DR. PORTIER: Dr. Tollefson, if you could please summarize.

DR. TOLLEFSON: Okay. And transgenic is going to fit that same purchase pattern. A winter decision and a spring application.

I apologize -- I'm done.

DR. PORTIER: For the record, my note here is that you are speaking on behalf of Iowa state University.

Could you clarify that for me?

DR. TOLLEFSON: I'm a -- well, I'm a

Professor of Entomology at Iowa State University.

DR. PORTIER: But, who are you speaking on behalf of?

DR. TOLLEFSON: I'm speaking as a scientist from Iowa State University. I'm sorry if I -- if you are misled. I cannot speak for Iowa State University.

DR. PORTIER: No. I'm not misled. I just want to make sure we don't mislead anyone else.

DR. TOLLEFSON: For the record.

DR. PORTIER: For the record, are you speaking for yourself.

DR. TOLLEFSON: Correct.

DR. PORTIER: Thank you.

Are there any questions from the panel, please?

Dr. Caprio.

DR. CAPRIO: You mentioned a figure of 15 percent dispersal. Is that primarily focused on prepositional females or is that spread evenly across the adult life span or is there a time frame when most of that occurs?

DR. TOLLEFSON: The numbers that I spoke about, we were flying females from essentially age 2 to 3 days old up until about age 15 days old. They were all pre-ovipositional. Maximum flight activity occurred at 9 days of age and it declined as ovaries began to development.

DR. PORTIER: Dr. Andow.

DR. ANDOW: Do you have any information on whether dispersal of adults is density dependent, do they dispense more from high-dense fields than -- you know, high-density fields and low-density fields?

DR. TOLLEFSON: I do not have any research evident that would support any of those. The only empirical evidence I have is when we've bombed miserably when we had a heavily infested field with beetles and next year we have very low larva populations, indicating that they probably left the field for some reason. But that would be an empirical observation not research.

DR. PORTIER: Dr. Weiss.

DR. WEISS: John, I have two questions.

On migrational flights of females, you just tested non-mated females?

DR. TOLLEFSON: I'm probably going to defer on that, because right now we hold females with males and then fly them. I'm thinking in the Coats and Tollefson paper we did the same thing.

We held individual pails of males and females and allowed them to mate and then flew the females and then dissected those females when they came off the mill to look for ovarian -- for mating. But I'm going to have to look that up for you.

DR. WEISS: Females that are gravid, do we have information on -- do they make migrational flights? You mentioned once the ovaries start to develop, that the migration flights tend to drop off and it is more trivial movement.

DR. TOLLEFSON: I can't answer that question because we terminated our flights at 15 days in the females.

DR. WEISS: But they had been mated or

you think they had been mated?

DR. TOLLEFSON: Yes. Yes.

DR. WEISS: By 15 days you would expect that some of them would have been gravid.

DR. TOLLEFSON: We also did a JH study along with it -- Juvenile Hormone, I'm sorry, and we found we could change the propensity of the insect to migrate by applications of JH and anti-JH.

The conclusion was as the JH levels increase and ovaries are developing, that the potential for -- or the interest in dispersing declines. We could suppress that declining by applying anti-JH and allowing -- then the females would continue to fly longer.

DR. WEISS: On an unrelated question, can you go over the 1 to 3 scale and what is a 1, what is a 2, what is a 3?

DR. TOLLEFSON: It is -- the scale that you are referring to is a 0 to 3 scale, not a 1 to 3 scale?

DR. WEISS: 0 to 3.

DR. TOLLEFSON: It is called a "No injury scale." It is a term we have coined. It is intuitive, because zero is no damage. Three is three nodes completely destroyed. One is 1 node gone, two is 2 nodes gone and any proportion of a node in between is listed as percentage. So 1.5 is 1 and a half nodes gone and a .5 would be how many nodes gone?

DR. WEISS: I would believe half. I went to Nebraska, but I think I can figure that out.

DR. TOLLEFSON: It's more intuitive than the 1 to 6.

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: Hi, John. The NCR 46 Committee -- how many scientists does that represent?

DR. TOLLEFSON: The reason I'm hesitating we used to consist of a voting membership of about 11 or 12 scientists, but that membership is expanding. It is now around 14 or 15 because we have picked up Cornell and Calvin at Penn State and so forth.

DR. HELLMICH: How many cooperators would there be?

DR. TOLLEFSON: I'm not giving you a specific number. There are two mailing lists that Lance Mikey would have right and Chris Defonzo, (ph) and those would be the mailing lists that would give those numbers.

DR. HELLMICH: The reason I'm saying that is because the communications from NCR 46 that have been mad to this committee, I think are very important because it is the collective experience of several corn rootworm scientists.

I think there is only one person on this panel that has actually participated in that and that's Bruce.

So I would like the committee to consider the recommendations from this committee very highly.

Also, I would like to commend NCR 46 for the leadership they have shown in working with NC 205 Committee and growers in trying to develop resistant management plans. I think it has been highly commendable.

I would like to suggest that you not go too far away, because they will probably have lots of questions for you because as I understand, have you had a lot of experience with this product.

Is that true?

DR. TOLLEFSON: I have worked with the product for three years. I have to leave to teach tomorrow. I mean, I'll be here today, I teach tomorrow. I don't know if -- but, NCR 46 is still around.

DR. HELLMICH: Thanks.

DR. PORTIER: Dr. Whalon, then Dr. Neal.

DR. WHALON: I would like to follow-up with a couple questions. You introduced the concept of a disynchronous trap crop idea as a monitoring tool. I wonder if you would elaborate on that?

DR. TOLLEFSON: The practice that we used to encourage rootworm infestations for research purposes is a delayed planting of corn.

With the later maturing corn being more attractive to insects when they are -- basically their hosts are synonymizing in the other fields, the beetle tend to accumulate in those trap crops.

I really intend to use the word, "accumulate." I don't believe there is an intentional movement of the insect -- directional movement to that field. I think it has to do with statistical result of frequency of leaving and longer stays.

What will happen is essentially is that late planted corn accumulates rootworms and we are able to do research under intensive pressures.

The reason I hesitate a little bit and qualified my initial statement is that I have no idea over what distances those beetles would be coming into that and what gene pool we're sampling with in the sentinel field.

DR. WHALON: Thanks for elaborating.

The next question is another elaboration and that is, you addressed maybe higher than expected selection pressure in some kinds of worst scenarios.

I wonder if you would elaborate on that?

DR. TOLLEFSON: I raise that issue because for example right now we're doing a research project in which we're evaluating an area-wide pest management concept.

In Iowa -- well, the state sites that are being done in Eastern Illinois, Iowa and Kansas are all 16-square miles in size. Our site in Iowa is 16-square miles. That includes 10,000 acres of cropland in it. The reason we chose that site it was it was one that had a heavy rootworm pressure in it.

And one thing that is unique about that area is that there are about 6,000 acres of corn grown continuously in a mon-culture out of those 10,000 acres. That is not typical of the statewide average.

In Iowa State an average of corn grown continuously is probably between 17 to 20 percent. We have about 12 million acres of corn and 10 million acres of soybeans that are rotated with it.

So, this area is unusual in that it is more intensively planted to corn following corn. As a result, it has more rootworm problems probably than some of the other areas, as Ms. Inman spoke about earlier where they do more rotation.

DR. WHALON: I would like you to just talk about monitoring a moment and talk about converting trap counts out of soybean fields to root injury the following year -- strategy for another monitoring system.

DR. TOLLEFSON: The problem we have had in monitoring when you are talking about relating adult numbers for one season --

DR. WHALON: Correct.

DR. TOLLEFSON: -- to the larval numbers or injury the following year? Usually, that equates to about a -- you expand about a third of the variation in rootworm larval damage in numbers based on the number of adult corn rootworms that were there the previous year. We're talking about

R squares of about .33 to .35. So, it is not very good.

DR. WHALON: Thanks.

DR. PORTIER: Dr. Neal.

DR. NEAL: Dr. Tollefson, you mentioned earlier that you thought it would be difficult to detect resistance based on root rating.

And could you elaborate on that and with some of the models the starting point is resistance gene frequency of .001 and what frequency of resistant beetles would you have to have in the field before they started making an impact on root rating?

DR. TOLLEFSON: Difficulty that I perceive in detecting resistance using root ratings or whatever, basically is first of all, we have variability in corn grown population densities from year to year. We're coming off about two seasons of very high rootworm population densities.

And at times, when populations are high, all the lodging that occurs gets blames on corn rootworms. So, windstorms will -- for example cause corn lodge and will be attributed to corn rootworm infestations and unacceptable injury.

And then when you go into a field and try to do the evaluation using root rating scale, basically, it is -- it take as little practice to be able to, if you will -- a calibration, if you will, to be able to apply those rating scales uniformly, especially if you are talking about rating at a very -- when I say "very," with a great deal of precision -- when we rate the MON 863 event, we assign root ratings on 0 to 3 scale, typically of a .02 to .05, which on that rating scale is essentially very slight grazing.

It is probably not likely, I would suggest, that a grower is going to see rootworm injury until they get to the rating of a .25, which would be essentially 2 or 3 roots that are removed from the plant and then it becomes more obvious.

You are to get a -- have to get a shift from scarring on the root tissue up to probably a quarter node gone before it actually can be detected. I don't know what that's going to mean as far as changes in gene frequency. I can't answer that part of your question.

Another problem is going to be that have you about the 25 percent survival on MON 863 in our experiments, so you are going to have a resident population of individuals in that field grazing slightly on the roots anyhow.

And those are -- that's the phenol-type of the insect and trying to pick out a resistant genotype with that background noise of susceptible phenol-types in there I think is going to be difficult.

DR. NEAL: Now, one alternative you mentioned was the sentinel fields.

Are there other ways of monitoring for resistant beetles? I mean, would one expect that the resistant beetles would have less of a delay in emergence?

Could you comment on what your observations are in delayed emergence of adults?

DR. TOLLEFSON: Our experience in delayed emergence on adults on the MON 863 event is similar to what have you have already heard. We get that same type of a ten-day delay.

I'm not exactly sure how I would try to translate into that into a resistance monitoring program, partly because of the extended emergence period of the insect.

DR. PORTIER: Any other questions?

Dr. Hellmich.

DR. HELLMICH: I really appreciate your expertise here to help us out.

DR. PORTIER: Dr. Gould.

DR. GOULD: I have a few questions.

When you were talking about the ten-day delay, that has been mentioned a number of times, but I'm wondering about the beetles that do come out ten-days later.

Have you ever seen anything that you would consider a sublethal effect? I mean, are the beetles the same size as they would be if they had been on regular corn?

DR. TOLLEFSON: Yes.

DR. GOULD: They are? Have you done any studies to see if their fecundity and everything would be equal?

DR. TOLLEFSON: Yes.

DR. GOULD: Great.

DR. TOLLEFSON: I are have a Ph.D. student right now that is looking at fitness and he's using a flight mail to look at their flight behavior and also collecting eggs to look at their fecundity and went back now, because of the questions you raised and looked at weights -- beetle weights and head capsule widths.

We're not finding any differences in body weights or in head capsule widths on the insect.

DR. GOULD: That's really helpful.

You were mentioning about the females moving more than the males. I mean, the data used in the models -- two models differ.

One is saying the females move times as much and one saying the females move four times as much as the males among fields.

Do have you some kind of feeling for that? Is that all within the range of what you have seen?

DR. TOLLEFSON: My experience in the past has been that I have seen very little long-distance dispersal in males. The females -- we get periodicity in their movement -- isodyneral (ph) periodicity.

We get the longer-range movement that tends to happen during those prepustular periods. With males we tend to see trivial movement that happens through a 24-hour period.

Having seen that in the past, I will admit we did not focus too much on male movement. We're doing some of that now with flight -- we're looking at male flight activity.

DR. GOULD: This is pretty critical to these models. I think what they were relying on in some cases was arrival of males and females in rotated fields.

Is that an useful technique or not? So,

you know, when you would measure the ratio of males and females in a field or arrival you would see different numbers to?

DR. TOLLEFSON: To me, I think that was important because of the previous studies that showed that we had predominately females in rotated corn fields, led me to believe that it was -- that 15 percent of the female population that really has interest in long range movement -- what Susan called in our paper -- those are the colonizers, those are the one that distribute the genotype throughout habitual environment.

Those are the ones that keep the species alive and well. That's predominantly the female that we see doing that.

DR. GOULD: Right, but the ratios that they report are about right then -- the 1 to 4 or 1 to 2 ratio of --

DR. TOLLEFSON: I probably wouldn't go that high. I'm hedging, because we'll have better information for sure when we flight these males.

DR. GOULD: And another question.

This is going back to what you said about the corn rootworm group in the letter that they sent. I think that they felt that a 20 percent refuge was appropriate.

Is that what I gather from that letter?

DR. TOLLEFSON: Our understanding -- the NCR 46 -- I'm going to try to be a little careful here because those of us on the subcommittee agreed that no one person can speak collectively for all the NCR 46 members, especially extemporaneously like this. So, I'm going to try be a little bit circumspect.

Based on the presentation of the model by the modelers that we have at the NCR 46 committee meetings, it was our interpretation of those model results that 20 percent refuge would probably be adequate for the interim period.

DR. GOULD: When are you considering a 20 percent refuge does that mean that 20 percent refuge is maintained in the same location year after year?

DR. TOLLEFSON: No. The NCR 46

Committee felt that it was important because of movement issues that the refuge be closer than the LEP (ph) refuge of a half mile, which was originally proposed.

We felt it would be better to have that refuge within the same field so it would be treated the same.

But I don't know of anybody -- the modelers are the ones -- the model results seem to indicate that keeping the refuge in a same spot is an advantage. The NCR 46, I don't believe, understood that.

DR. GOULD: That depends on that male movement. That's why I'm asking that.

DR. TOLLEFSON: Yes.

DR. GOULD: A final questions is -- I mean, you do farmers and you do extension kind of things. I mean, do you think farmers would keep the refuge in the same place year after year if they had continuous corn production?

DR. TOLLEFSON: There are previous speakers that would have more experience --

DR. GOULD: Yes. Sorry.

DR. TOLLEFSON: -- for that and my estimate would be, I don't see any reason why they would be able to do that. Have you heard some of the issues surrounding corn plant or clean out and things like that and when are you talking about a refuge that's fairly sized -- considerable size, that those refuges probably would be able to be kept in a very similar system.

DR. GOULD: I'm thinking about damage in those refuges.

DR. PORTIER: Excuse me, I'm going to want to remind the panel to please keep this a little bit shorter. We're starting to run very, very long over in this. Try to crisp questions with crisp answers.

Dr. Gould.

DR. GOULD: Okay.

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: John, I agree with you that this no injury scale is simpler and maybe a more efficient way to rate damage.

What are the typical root ratings that you would get with the MON 863 if there is pretty heavy rootworm pressure?

DR. TOLLEFSON: This year we had rootworm pressure that was heavy enough that our susceptible line was literally in danger of dying prior to the July 4th, ran, we got four inches. Those infestations are MON 863 rates, as I said, .02 to .05, which is scarring on the roots.

DR. HELLMICH: Typically, if you have -- how does that .2 to .5 with this product compare with .2 to .5 with another product? Is the damage -- does it look different?

Do you just get grazing on the outside or if I had a root that was rated the same and I brought them to you, would you be able to tell which one was 863 versus a non-Bt just based on the characteristic feeding?

DR. TOLLEFSON: No, I would not.

DR. PORTIER: Any the other questions by the panel?

Dr. Neal.

DR. NEAL: One further question on rootworm movement. Are there differences in the rates of movement in different populations of western corn rootworm and here I'm thinking far-western part of the corn belt versus the eastern part.

DR. TOLLEFSON: I wouldn't have any basis to answer that question. The only insects we have been flown have been Iowa insects.

DR. PORTIER: Thank you very much, Dr. Tollefson.

Dr. Teresa Gruber.

DR. GRUBER: Good afternoon. I and Teresa Gruber from the Council for Agricultural Science and Technology. CAST is a nonprofit, non advocacy membership organization governed by a board of directors comprised of representatives of 37 scientific societies and one representative of individual members of CAST.

I'm pleased to be here today and to bring to you not only my comments but a copy of a recent report that CAST published entitled "The

Comparative Environmental Impacts of Biotechnology Derived Soybean, Corn and Cotton Crops."

In addition, we have for you a copy of the CAST policy statement on food and agricultural biotechnology.

I would like to give just some overview comments on the risks and benefits of food and ago-cultural (ph) biotechnology before I address just a few of the questions that EPA has posed to your panel.

First CAST believes that all technologies, including biotechnology, must be evaluated in light of the consequences of their implementation or of their non-implementation and must be compared to the safety of alternative technologies.

Evaluations of risks and benefits must be placed into the context of current and historical practices as well as impacts on human, animal and environmental health.

We feel that the adoption of Bt corn for rootworm control will likely have significant environmental benefits relative to conventional corn systems in the reduction of insecticide use after planting, which should result in reduced human exposure to harmful toxins and greater efficiencies in land and energy use.

We see a need to study the impact on soil organisms and insect resistance management of the coupling of insecticide treated Bt corn seed to control other soil pests with corn rootworm technology.

Such studies should be designed to detect pest population shifts which may occur as normal soil insecticide use decreases and treated or untreated biotech enhanced seed is planted.

We believe the EPA has identified and considered a reasonable and rational set of taxa and species for pest incorporated protectants.

Tests and resulting decisions should emphasize concentrations of the toxin likely to be encountered by natural enemies and other non-target organisms under natural or field conditions.

Now, comments regarding resistance management in particular.

I would like to first to address very briefly pest biology research and let you know that we think a resistance management plan depends on species specific and environment specific information concerning toxicology and behavior of the targeted insect.

Lethal and sublethal affects can vary from species to species and dispersal and mating behavior do vary across environments species.

We would add that corn rootworm protected corn can be a useful tool to counteract the resistance to crop rotation that has already developed in corn rootworm.

A second topic regarding dose -- CAST recommends studies to determine the effective dose of the biotech derived corn rootworm protected corn. These studies may assist in the development of strategies for the elimination of density affects.

Also, the change in dose in the roots

over the larval period should be measured to determine if the toxin concentration starts at a very high level and then declines.

Therefore, additional studies should focus on larva rather than measurement of emergent adults.

A third area on modeling.

We draw attention as has already been done to the only published model of western corn rootworm and transgenic corn done by Olstad and others which indicates that first with complete adoption of technology by growers and block refuges and planting the refuge in the same place year after year, the time to reach 3 percent resistance allele frequency varies from 5 to over 100 years, depending on the true dose and toxicity unless the resistant allele is completely recessive, in which case it is unlikely that resistance would ever develop.

If the expression of the resistance allele is dominant, then resistance will occur very rapidly after complete adoption of the technology by farmers.

Where block refuge is planted with a field and in different locations each year, the development of resistance should be closer to that simulated with refuges as row strips.

In that case, Olstad and his colleagues found that the rapid development of resistance compared to the external and non rotated block refuge is due to the greater proportion of eggs oviposited in what later becomes the corn rootworm protected Bt corn the next year.

Moving onto monitoring. I just have some general comments that CAST does advocate a careful and objective science-based evaluation.

I think we probably all agree on that -- an evaluation of the technologies and products of biotechnology through continuous testing and safety assessments for reasonably foreseeable risks.

Also, continued implementation of appropriate bio-safety and environmental controls, a frequent review of safety evaluation procedures and economic and benefits assessments.

CAST recognizes that there is stakeholder involvement in regulatory oversight at each stage of development from concept to post-market stewardship.

We further recognize that conditions of registration and continued registration can and should minimize reasonably foreseeable risks while maintaining access to food production and agricultural practices, which can contribute to quality of life by improving food security, health care and the environment.

Therefore, we encourage frequent review of the safety assessment process and of biotech derived crops approved for commercialization to ensure that the process continues to use the best available scientific data and assessment practices and to ensure continued safety in planting and use of biotechnology derived crops.

Again, I would like to thank you for the opportunity to be here with you and to answer questions to extent I can. I would also like to acknowledge David Olstad who assisted us in preparing comments today.

DR. PORTIER: Thank you Dr. Gruber.

Are there any questions from did panel?

Yes, Dr. Neal.

DR. NEAL: I had one question on a statement you made that dispersal and mating behavior vary across environment in species and is there a particular piece of data that this is based on or is it a general statement?

DR. GRUBER: I don't -- I think it is a general statement on my behalf. It is very possible that Dr. Olstad may have more specified studies that he would refer you to and he has agreed to be available to talk to any of you by phone or to follow up on more detailed questions.

DR. NEAL: Thank you.

DR. PORTIER: Are there any other questions?

Thank you very much.

DR. PORTIER: Let me ask a quick question of the panel.

Yesterday when we went through the Q and A's with the representative from Monsanto, it took us almost an hour.

And I don't want to shorten our discussion if there are specific inquiries with the Monsanto group.

Do you foresee a lot of questions for the Monsanto presenter? Yes; I see a lot of nodding heads here.

So, then I'm going to take the Chairs's prerogative and I'm go to go switch the order of presentations of the public comments. Right now I would like to ask Doug Gene Sherman (ph) to make their comment and then we'll go on beyond that.

DR. SHERMAN: I would like to add my thanks to both EPA and the panel for taking the time to do this task. It is a very important task and would also reiterate that EPA is a leader in its transparency and openness in these processes and is a very important function.

I'm Doug G. Sherman, the Science Director for the Biotechnology project at Center for Science in the Public Interest. We are an advocacy organization that is primarily concerned with nutrition and food safety issues.

We're also concerned about environmental issues in the area of crop biotechnology.

I would like to just preface my comments very briefly with comment directed towards -- Dr. Federici commented this morning on non-targets in question two.

I have circulated, I think to all of the panel members, comments that we have submitted to EPA. So, I'm not -- certainly not going to spend any time on that except to say that we do share the concern that was expressed about the field data and other data and would want that considered in the record.

We do also think that Bt crops and the Bt resistance genes, based on what we understand about them often have the potential to have lower impacts than certainly some insecticides.

We would expect it to have -- be much safer to farmers and farm workers certainly than the OPs that are currently used to control corn rootworm now. So, to the extent that they replace those, I think would be a good thing.

I also would like to briefly comment on what we think is a general issue that is of importance that was, I think implied by what Dr. Federici said and also to follow-up on some comments that Dr. Portier mentioned that we think it's critical for the Agency to move forward on developing -- that is, detailed guidance for companies as possible.

I think some of the issues that came up about inadequacies in field studies could be better addressed by everybody if up front there were adequate guidance that gave everybody the needed instruction on what would be adequate up-front rather than down the line.

We do think that the SAPs that have been conducted, as well as the recent non-target workshops are a good step in that direction. We would encourage EPA to continue seriously working towards a better guidance for everybody.

In terms of resistance management, we also share the concerns that not enough is known as anybody would like about the biology of corn rootworm. I don't want to belabor some of the issues that have already been brought up.

Again, they are in our comments. But I would like to emphasize just a couple issues that have been touched on by several speakers and are of concern to us as well. One is the assumptions that are made about adoption of corn, corn rootworm protected corn.

I think we have heard different things and different assumptions about how quickly it will be adapted locally.

I think the concern about local adoption and development of resistance is an important one, rather than focusing on just the state level or national level.

We consider the local level more acceptable hybrids to certain local conditions may be available more quickly. And I think that needs to be seriously considered.

Also, clearly, some of the parameters that are important to the models that have been developed, we know very little about apparently. I'm out of my depth here I admit it I'm a plant pathologist not an entomologist.

But parameters like resistance to allele frequency -- my understanding is we know virtually nothing about and they can be very important in terms of the rate of resistance development.

Another issue around local development -- around local adoption that we're concerned about is other products that may came on market fairly quickly, especially other generically engineered products.

We don't know a great deal about those products and somebody who does know -- maybe an EPA or on the panel can correct me if I'm not correct on this -- but at least one of the other products is based on a Bt gene. I haven't heard anything about the potential for cross resistance between Cry3Bb1 and that product.

I don't know if there is anything known about potential for cross resistance, but rate of adoption when that comes on line will certainly impinge on the efficacy of resistance management.

Just to conclude, I think because of the limitations on what we know about the biology of the insect grower adoption and previous lack or less than desirable implementation of the refuge strategies which have by survey been indicated to be more like 80 or -- 70 to 80 percent in the past that we need to take a very conservative approach to how resistance is managed if the agency decides that this product is safe and goes forward with it.

If it is safe, it needs to be conserved for long term use and I think, therefore a conservative approach is needed at least until there is more information about the biology of this organism.

We would reiterate the proposal that larger refuges are considered but also restrictions on local sales that would prevent large local areas from being grown in this crop in the near term.

Thank you.

DR. PORTIER: Thank you Dr. Sherman.

Are there any questions from the panel?

No questions at all? Thank you very much.

According to my clock, it's 12:24. Rather than go that the final public commentator, which would be Dr. Vaughn from Monsanto, I think we will delay that public comment until after lunch and begin our session right after lunch with the public comment from Monsanto.

I would hope that Dr. Vaughn will be prepared to start at exactly 1:30, with the projector all set up.

Does EPA have any questions relating to any of the public comments so far?

DR. ANDERSEN: No, I don't think so. Thank you.

DR. PORTIER: Then with that, I think I will close this morning session and we will begin again at 1:30 promptly.

Thank you very much.

(Thereupon, a luncheon recess was taken.)

DR. PORTIER: We ended the morning session with one remaining public commentator and we are going to start the afternoon session with that comment now.

Dr. Vaughn.

DR. VAUGHN: Thank you and members of the panel, thank you for this opportunity today. My name is Dr. Ty Vaughn. Just a brief synopsis of my background. I got my Ph.D. From Colorado State.

I worked in an area of population genetics at the time working on movement of parasitoid wasps and aphid species in agricultural settings.

I then went on and did a four-year post doc at Washington University in St. Louis, where I did mapping of QTLs concerning quantitative traits of different phenotypes.

Currently, at Monsanto, I'm research entomologist where I am responsible for the research and research collaboration surrounding MOB 863 and the insect resistant management plan for that product.

We've been actively working on developing a resistance management strategy for MON 863 since 1998. It was in fact part of a product concept.

The interim plan was developed from the direct experience that Monsanto has had with other Bt products. There was also a collaborative effort with University and government scientists who are experts with corn rootworm biology management and IRM in general.

The outcome of these collaborations is the interim plan that you have before you and it has been submitted to the EPA in support of MON 863.

Like I said, it has been a plan that was developed within put from the nations leading corn rootworm experts, NCR 46, and I think Dr. Tollefson alleged to that this morning.

This group of scientists has provided

EPA with a rigorous assessment of the IRM plan and found that it is acceptable for an interim period of time.

Today I, would like to focus the comments on specific aspects of the resistant management plan that has been proposed and there are five areas I would like to cover.

The first is just the interim nature of the proposed plan and why we think that that's an appropriate way to proceed.

The second is the approach to the structured refuge size and placement and get into some of the details that we have heard a little bit about this morning. Number three, the performance or the dose of MON 863. I will pickup some more details there.

The fourth then would be the practicality and flexibility considerations that were incorporated into this plan as it was being developed and then the fifth, we'll cover just briefly some of the ongoing research that we hope to obtain during this interim period.

To begin, I want to emphasize that Monsanto recognizes that any IRM plan will necessarily need to strike a balance between current and technical knowledge and grower practicality.

We're proposing a three-year interim plan for corn hybrids containing MON 863. That includes a 20 percent structured refuge, placed within or adjacent to the MON 863 field. This plan was intend today limit overall selection pressure from MON 863 on corn rootworm populations during that period of time.

A proposed interim plan incorporates what is know about the biology of the target, pests, the growers needs, the dose of the product and product adoption patterns.

It is also important to realize that the data currently available are sufficient to design a low-risk IRM plan while additional data are collected.

For example, there are some questions related to the interaction of the biology of the corn rootworm and MON 863 that can only be answered after commercialization such as the precise understanding of insect plant interactions into the commercial scale uses.

We recognize this and as a result, we've proposed am interim plan that is conservative and supported by the data that we have available to us today.

A deployment of the structured refuge and combination with factors that limit levels penetration during initial years on the market and the availability and use of other management strategies that growers currently use such as rotation and chemistries, will, in fact limit overall selection pressure on Cry3Bb1.

I would like to move to more detailed focus of the structural elements now of the interim plan, including the placement and size of that refuge.

I want to underscore that these structural elements were designed specifically to take a conservative approach during this interim period.

So the plan includes a requirement of the 20 percent refuge associate each MON 863 field. The refuge size is based on two principal considerations.

The first, we use simulation models to assess the relative important of refuge using a range of conservative estimates of important parameters such as the level of adaption, the degree of dominance of the resistive allele, the range of dose levels, and other parameters.

These models indicated that the size of the refuge is relatively unimportant for determining overall durability of low to moderate dose products. The goal with these models was not really to predict durability necessarily, but to help guide our research strategy.

So, we heard from Dr. Storer this morning where he was looking at the adaptation rates. With that model that he was using it didn't accurately characterize product characteristics of MON 863.

I'll get into a little bit more of that in just a minute, but I think that's important when we're trying to evaluate models that they have as much as we know about these products and incorporation into them from the beginning.

The second part of this is that the 20 percent refuge is designed to facilitate grower compliance. As this refuge is familiar to growers who currently use other Bt products and that familiarity increases the likelihood of grower compliance with IRM requirements when MON 863 hybrids are planted.

So, in addition to that, they would also be a much larger defacto refuge that will exist during this period of time while the plan is in effect.

While the IRM plan does not explicitly rely on adoption rates, the use of MON 863 hybrids will be limited during the first few years following product launch, while new hybrids are introduced and evaluate by growers.

As we heard one grower this morning, it

is all about the yield in the end. They need to understand that before they would fully adopt this product.

The IRM plan requires that the growers plant refuges within or adjacent to MON 863.

It is currently understood and we have heard about it this morning as well that the movement of adult rootworm beetles before mating is limited and it indicates that the refuge should be in close proximity to the transgenic field to encourage random mating.

So, consequently corn rootworm experts, such as NCR 46 and the Canadian Corn Pest Collation have recommended that in field or adjacent options is the most appropriate to encourage that random mating process. Because the of the differences insect behavior, the half mile option refuge allowed for corn bore technology would not be appropriate in this case.

So the proposed plan differs from the plans in place for the existing corn bore technology, precisely in the distance requirements.

The third topic then is the performance of MON 863. I think Dr. Tollefson alluded to that this morning. The root damage ratings that are seen for MON 863 are very good. He quoted numbers .02 and .05.

These are excellent root damage ratings, although that does indicate that there is some scarring on the root tissue. While MON 863 does provide excellent corn rootworm larval feeding and plant -- from plant damage, it does allow corn rootworm survival in adult emergence levels similar to those that we have seen with soil applied insecticides in the past.

To date there is no evidence or resistance to soil insecticides the past 30 years, even without any resistant management strategies in place for those technologies.

So, why do so many beetles emerge from MON 863? I think the answer reflects a combination of several factors.

The first being the Cry3Bb1 itself has

relatively low activity against corn rootworm, especially when you compare this to European corn Cry3Bb1.

The second point here is that the behavioral response of corn rootworm larva to root of MON 863 plants is different than what we have seen in other Bt products with insects.

We heard earlier too that the larvae tend to graze on the corn rootworm on the corn roots and this provides the scarring in those damage ratings we have heard about -- this .02 to .05 are a direct result of that grazing over the entire corn root system.

So, the third part of this then is the substantial larva mortality caused by a number of highly variable and environmental factors.

These factors range from things like density dependence mortality, planting date and soil moistures and types that together can exert selection as strong or stronger than the selection exerted by MON 863, meaning that corn rootworm survival will often be more of a function of those factors than mortality solely related to just MON 863 or at least allow those selection factors to have a role in the overall selection process.

A fourth point I would like to talk about, we did hear some excellent remarks this morning from the growers, but we also saw input directly from growers to ensure that the plan that have we submitted is reasonable, practical and compatible with growers farming practices.

The opportunity for growers to realize the benefits of yield guard rootworm will be determined by how practical the IRM is for growers to implement.

Previous EPA scientific advisory panels have emphasized the importance of balancing the scientific components of IRM plans with practical considerations that are feasible to growers and easily incorporated into their farming practices.

Our experience with the Bt products used to control corn bore have demonstrated the importance of providing a flexible and practical plan to these growers.

Thus these considerations a critical part of the intern plan for MON 863, The last point then is the ongoing and planned research we have outlined in the IRM plan. It includes research that will help guide the development of long term resistance management strategy for this technology.

The plan itself is actually designed so that it can evolve and fit into the new knowledge that we gained during this phase.

So, for example, some of the studies we have ongoing are designed to understand dispersal using market technology and population genetics to better understand effective migration rates.

We also have ongoing studies to determine to the fitness of insects that are feed on MON 863 and how that fitness compares to insects that are feed on conventional hybrid corn.

There are also studies underway to examine more precisely the plant insect interactions to understand corn rootworm feeding behavior and survival on MON 863. These studies and many other that are underway are important components of the research program designed to support the long term resistance management strategy.

In conclusion, the interim plan is designed to provide a technically appropriate resistant management strategy that growers can implement.

The plan was developed with input from the nation's corn rootworm leading experts who have concluded that the plan is acceptable for the proposed interim period. With that, Mr. Chairman and members of the panel, I would like to thank you again for the opportunity to make comments on behalf of Monsanto related to IRM corn rootworm.

DR. PORTIER: Thank you Dr. Vaughn.

Are there any questions from the panel?

Dr. Whalon.

DR. WHALON: This is a carry over from one of the interactions we had with a grower before. But in your EUP releases, how were those seeds set up and what kind of comparisons are you running in those?

DR. VAUGHN: Under the EUP we have a wide variety of different kinds of trials. Maybe you are talking about efficacy trials in this case?

DR. WHALON: Right.

DR. VAUGHN: So, in the efficacy trials, we compare MON 863 to industry standards. These are insecticides that are commonly used in different regions of corn growing areas.

We compare these with and without seed treatments. So, in the case I think that you are mentioning of the Goucho seed treatment was used, we have run studies where we have conventional hybrids without any seed treatment.

We have with conventional hybrids with Goucho. We have MON 863 with no seed treatment. We have MON 863 with Goucho. This is a low rate of Goucho, only effective on secondary insects.

So, from those studies, we were able to show that the low rate of Goucho used in this case or other seed treatments has no impact on corn rootworm.

DR. WHALON: When a grower is looking at yield as the deciding criteria, basically, what is in his pocket at the end of the time and you've got a seed treatment and a non seed treatment variety side by side. It is not really a heads up comparison in a sense.

DR. VAUGHN: No. So, in those comparisons it would be the a seed treatment on both sets. So, we have MON 863 with the same seed treatment as on the conventional hybrid.

The other comparisons I was talking about solely reflect what impact might be on the corn rootworm from that seed treatment on corn rootworm only though.

DR. WHALON: Are there sublethal effects or anything like that on corn rootworm?

DR. VAUGHN: On Goucho, no.

DR. WHALON: How do you know?

DR. VAUGHN: Well, sublethal affects on the individuals of corn rootworm that survive, no.

This was looking at damage ratings and looking at adult emergence from cages of plants that were caged underneath those treatments.

DR. WHALON: It would be interesting to see that data.

DR. PORTIER: Any other questions from the panel?

Dr. Hubbard.

DR. HUBBARD: One of the questions proposed to the panel from the EPA was whether or not data collected for western corn rootworm are going to be applicable to northern corn rootworm, Mexican corn rootworm, and southern corn rootworm.

In your response to the -- in Monsanto's response to this question in your written responses, on of the -- I can quote -- "The southern corn rootworm is not adequately controlled by MON 863 under field conditions." That's a quote from your response.

So, if that is your response to this question, is it appropriate then to just remove southern corn rootworm from a label for this product.

DR. VAUGHN: Yes.

DR. PORTIER: Other questions?

Dr. Caprio.

DR. CAPRIO: Ty, you mentioned soil insecticides and that resistance is not developed in those over 30 years.

My understanding is that they tend to be very focused right where they put down that insecticide and there is a large number of roots that extend beyond that zone where there are insects emerging that have not been exposed to selection. So, there a spatial variability in that toxin.

Can you address that variability in toxin in the root system of these transgenic plants? Is it a uniform expression throughout the root system?

Is there variability in that toxin and if so how does that play in the comparisons of the soil insecticides versus the transgenic?

DR. VAUGHN: So, with the soil insecticides, I think there are two components. There is a spatial and temporal component to those. So, they have a narrower window of life in the soil.

And like you said, the only control within a band around that root zone. So, the roots that do grow beyond that band, that is resource that the corn rootworm then can survive on.

From MON 863 we have not seen any difference in expression level across the root zone.

But in effect, I think Dr. Storer mentioned it is this morning that those soil applied insecticides actually have a low dose and a built-in refuge at the same time.

So, with MON 863, while the expression doesn't change across the root zone as far as we can detect, it also is present during the entire life cycle of the insect development period.

DR. PORTIER: Other questions is?

Dr. Weiss.

DR. WEISS: Ty, going up, building on Bruce's question, do you have any data on the Mexican corn rootworm on this product?

DR. VAUGHN: We have very few data sets available right now. That insect is pretty sporadic, so we cant' really -- we don't really know where it is going to occur at any given year.

With the EUP requirements that we're under, we need to have those locations identified well in advance of understanding where the insects may appear. So we do have some limited efficacy data. So, we do have some limited efficacy data.

DR. WEISS: Is it similar to western corn rootworms.

DR. VAUGHN: It is similar to western northern, yes.

DR. PORTIER: Other questions?

Dr. Neal.

DR. NEAL: Yes. With one of our previous guests, Dr. Tollefson, he felt that root rating would not be a good method of detecting the appearance of resistance and I was wondering if you could address that point on detection of resistance and how you plan to do that.

DR. VAUGHN: Sure. So, the ability for a grower to detect resistance is going to be very difficult for them.

What we envision at least at this point is if a grower would see some unexpected damage which he would notice as perhaps extensive amount of lodging in his field, that would trigger a phone call and we would start to investigate that to make sure that the field that he had that problem in was, in fact, planted with MON 863.

So, we would start down a path that validated that the plants were indeed the plants that were intended to be planted there. But beyond that the root damage rating isn't very useful to growers.

They can be trained to understand what those root damage ratings mean, but again there is enough variability within that root damage rating and variating within the rate roots, that it would be a very difficult thing to try and put thresholds on.

So, where we're at with this is that we have started a monitoring baseline population susceptibility study where we're going to have baseline data built-in to the plan and we would rely on monitoring for changes in tolerances overtime.

So, that would be really where we're at with the monitoring for MON 863. We're going to be relying on bioassay data more so than unexpected damage or root damage ratings.

DR. NEAL: Could you he lap elaborate on how you conduct those test?

DR. VAUGHN: The baseline studies, sure. So, these are basically similar to how European corn bore studies have been conducted in the past.

And the person that has actually conducted this is Dr. Blair Sigfried, (ph), at the University of Nebraska.

We have been collecting individuals, populations from across different geographies now in the past two to three years, rearing them up over the winter periods and then putting them into bioassay during the summer of the following year.

Those assays are conducted with artificial diet, designed for corn rootworm growth, larval growth in the laboratory and then different dose response curves are run against those populations.

DR. WHALON: Could I follow-up on that issue?

DR. PORTIER; Sure.

DR. WHALON: When you run those, if you are going to select an environment like that to try to find resistant alleles from stock from the field, what kind of problems would you run into?

DR. VAUGHN: So, select from the bioassays?

DR. WHALON: I mean, select a large group through that mechanism, through the same kind of selection process you would put on or mortality mechanism you would put on in Petri dish kind of assay.

DR. VAUGHN: Sure. So, like I said to begin with, the difficulty in this in using something like that, using a protein bioassay-type design for creating resistance is that the protein itself is just not terribly active against the corn rootworm population in general, against those individuals.

So, I think the biggest problem that would be run into is that after a few generations of this, the concentration of the protein that we can actually provide to run these assays with, will become limited.

It is just not possible to get a high enough dose -- the Cry3Bb, to cause 10- or 100-fold increase in tolerance overtime. So, I think that creating resistant colonies using protein and bioassay is going to be very difficult.

DR. WHALON: Other problems too, with the larval growth on those media -- over growth of other organisms, micro organisms and stuff like that.

DR. VAUGHN: Yes. So, we have -- and this was the biggest hurdle that we had to deal with initially is that corn rootworm coming from the field are full of different kind of organisms.

Once you wash them out and try and disinfect everything that you can, you still end up with large amounts of this unintentional growth, whatever it might be -- different pathogens -- on that media, because it is designed to cause growth of the corn rootworm.

So, we do have procedures in place and actually the methodology of this has just been accepted into entomology, and should be out by the end of the year and this includes disinfecting the eggs and doing different things with the diet to try and limit that kind of growth and allow these assays to run. I think Dr. Sigfried can attest that the method that we've got in place now to run these bioassays works quite well.

DR. PORTIER: Dr. Hubbard.

DR. HUBBARD: To me one of the reason that the soil insecticides have not developed resistance in more than 30 years is that there is an infield refuge with a large number of susceptible beetles that are produced.

I believe that those beetles have experienced a low dose of insecticide, similar to what might be the case with MON 863.

The key question in my mind is whether the beetles produced from MON 863 are susceptible and as curious, if you have any data to this point verifying that those beetles that are produced are still susceptible or is there a 20 percent, 20 to 50 percent resistant background in the population?

DR. VAUGHN: So, those studies have not been conducted taking individuals that have survived MON 863 out in the field and put them into the laboratories. They are not complete, let me put it that way.

Dr. Lance Mikey is actually running that part of research strategy right now. He has a number of large screen house studies where he has planted MON 863, as well as ice lines and he has taken beetles that have survived from the MON 863 and put them back into a rearing program and started to look at the fitness parameters and other components of the beetles to understand what sort of impact they have had.

But to date, we haven't run laboratory diagnostic bioassays, dose response curves on those populations yet. The number of beetles that are generate from these kinds of studies are fairly small to try and run large-scale bioassay experiments on.

DR. PORTIER: Dr. Gould.

DR. GOULD: Throughout your documents and in your speech today, you keep saying that you have developed a conservative approach and that the data are -- there are enough data to develop a conservative approach. You may be confident in that but I certainly am not.

I would like to comment just a little bit also in terms of your comment that a refuge doesn't make a lot of difference for the moderate and low doses compared to the high doses.

That has been understood for a very long time and the problem is that you get resistance whether you do or do not have a refuge in those kind of cases.

One thing that hasn't been addressed here at all is quantitative genetic variation in your beetles. I don't know how are you dealing with that kind of problem. We're not talking about a low frequency but rather a very high frequency check.

I would just appreciate more comment on what that in terms of why you are claiming this to be a conservative approach.

DR. VAUGHN: The conservatism is really in this -- built into this interim plan. I don't want to dwell on the adoption argument at this point.

There are factors that are well documented and I think we heard some them this morning on how growers will adopt this technology and how they actually put it into their system to make sure it fits.

So, the conservatism -- maybe there is a range of conservatism on different parameters, but that is one level of it. We have also decided that this 20 percent refuge will also augment -- and the 20 percent refuge structured and placed within the field encourages the random mating process.

So, that again leads you down the road of, this is still building in conservatism without going -- without making it too impractical for growers to implement.

As far the quantitative genetic architecture of these beetles that are surviving, that is one of the unknowns and that is one of the things that we hope that we have some research -- ongoing research strategies to try and development.

As you well know, those aren't easy assays or population experiments to run. Those are very difficult and I'm note even sure at this point if there are other pest populations that are exposed to transgenic plants, that that information is identified without any doubt.

There are well document examples in nature of this sort of thing happening with low-dose products -- not products, low-dose plants with herbivores on them.

In most of those cases, what tends to be the case is that the mechanism of resistance is not a single gene. It tends to be a number of genes, a polygenic trait. What we know from quantitative genetics is that things that cause adaptation against a polygenic trait seem to take a much longer time than they do if they are monogenic -- if it's monogenic in the process.

So, we're talking about the Fisher-Wright (ph) argument at this point.

In essence, we don't know the level of dominance. We know if you have a high-dose product that you force an effective dominance level -- force an effective recessive allele frequency anyway.

With a low-dose product you don't, and

so are you not forcing it to fit into that model in this case. It is going to be the natural variation in number of resistance wheels in that population are going to be there, because we're not calling them out because it is not high dose.

I'm not sure if I answered everything you asked.

DR. HUBBARD: I wanted to hear more about the conservative approach.

DR. PORTIER: Other questions?

Dr. Andow.

DR. ANDOW: Bruce Hubbard's question seems to me to be quite critical in terms of, is there already resistance or not?

Getting a clear answer to that would seem to be very important, because if it does turn out even if there is quantitative resistance and your are getting some response to the selection, then it sort of throws a lot of interim plan into question as to whether or not it will even work.

So, it seems like deciding whether the interim plan really is conservative depends a lots on the results from those experiments. To me, I would like to hear what you are thoughts are that.

DR. VAUGHN: Another part of the conservatism is also in the biology of the insect. Having only one generation per year, we wouldn't expect to see resistance developing in three generations in this case. None of the models, even under worst case situations like some of those that Nick presented this morning even show that.

So, we don't believe that during this interim period, that there is going to be enough selection pressure in any given population that it would put an interim plan in any sort of risk.

That's why we called it low risk. The kinds of studies you are talking again, I think are what Dr. Gould was talking about too, trying to understand the genetic architecture of resistance under a low-dose situation is complicated enough.

Designing that experiment is going to take some real thought. And implementing that is also going to require a lot of discussion as well.

DR. ANDOW: I guess my question was not quite as sweeping as that.

It was basically, if Lance finds out that after one generation of selection that there actually is increased resistance in that population, do you feel that this interim plan then is appropriate to persist with?

DR. VAUGHN: In this case too, he has got something that is very close to a natural situation. These are greenhouse studies with real plants growing in real soil taken from the field. What is limiting the selection here or what would be increasing selection in this case, is that the environmental conditions are very good.

The plants are going to be well watered, moisture soil-types these sorts of things are going to be well maintained in the field under natural situation. That may not be the case, so the other components -- the environmental stochasticity is also going play an important role.

So, if beetles emerge he brings them into bioassay and we just don't know at this point if we are ever going to be able to do that with this kind of an assay, because of the limited numbers that are actually produced under these 10 by 10 boxes essentially, in a greenhouse.

Will we get enough beetles to actually do those kinds of experiments or will it take collecting beetles out of fields under larger field trials.

DR. ANDOW: I have three smaller questions.

One is, do you ever see root tunneling by the larvae inside the major roots?

DR. VAUGHN: The MON 863? No.

DR. ANDOW: So, if there is even one incidence of root tunneling, that would be unexpected.

DR. VAUGHN: Under the highest pressure situations and we have only really seen some of that this year and the data are just coming in from some of these areas where root pressure --

root damage -- or corn rootworm pressure was really high, I would expect that if we saw large amounts of tunneling we could verify it was due to only corn rootworm, then we would certainly be looking into that.

DR. ANDOW: Well, I just asked if you have seen one instance, one root being tunneled.

DR. VAUGHN: I'm not aware of that, no.

DR. ANDOW: That's why I'm saying that would be unexpected to see one tunnel.

The other question is there any evidence of adulticidal activity of the MON 863 event? I keep hearing back and forth. I understand these isn't but --

DR. VAUGHN: We have not seen any against adults. We have looked at instances of silk clipping and a number of beetles on plants on the field and we have also looked at -- again at Dr. Sigfried has looked at feeding Cry3B bt to corn rootworm adults and have found no impact on the adults.

DR. ANDOW: The last question is,

supposing that this interim plan is allowed and three years from now we have information that suggests changes to the plan, do you have in mind any contingency plans for how to go about doing those kind of changes?

It would seem like if there is no plan to make any changes, then it may be difficult to make the changes.

But if it really, truly is an interim plan, then one might be want to be planning for the possible -- possibility that there will be changes, including informing growers that there that is some likelihood that things will change in years and so on.

DR. VAUGHN: So, the data that will be generated over those years. It could be that individuals that emerge off of MON 863 have undergone enough changes in activities in their behaviors such as even dispersal that the perhaps the refuge -- the structured refuge near the field could be moved a further distance or the structured refuge might not be necessary.

There are lots of possibilities. Perhaps, where you are going is -- are there changes where we're going to be informing growers that the IRM plan we have told them about initially will change.

We have an ongoing education program that we have started already with growers, to help them understand already the difference that we have made from corn bore technology. So they understand that the refuge will have to be placed closer to the MON 863 field.

We're building that network now to help growers understand and educate them as this technology comes into play in the market place.

DR. ANDOW: I guess my question was more -- are you also targeting information to them that in three years this could change?

DR. VAUGHN: Yes. Oh, definitely. We have told them that this is proposed plan. We haven't told them that this is the plan at this point.

We're telling them that we've proposed a plan, because we wanted to engage their feedback on how they could implement something like this.

Does planting a refuge only within your MON 863 fields, how does that impact your economic practices. What we learned was that about a third of them said that under those situations they would have a very difficult time implementing this.

So, yes; we have been telling them all along that the plan is a proposed plan and that we're moving forward with this plan because we believe that this is the best case situation for them and doesn't impact their ability to use this technology.

DR. ANDOW: Thank you.

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: Dr. Vaughn, I have a few questions here.

Have you tested third-in-stars versus first-in-stars and their susceptibility to the protein? If you have is there any difference?

DR. VAUGHN: Yes. We have tested for

second and third in stars against the protein and against first in stars, we really -- we see we can derive an LC 50 from that.

Second and third in stars, we cannot. We see no mortality even at the highest doses. We do see some delay in growth when we look at the development stages overtime, but we don't see any mortality against second and third-in starts.

DR. HELLMICH: Are corn bores -- or rootworms -- are they cannibalistic at all?

DR. VAUGHN: Not that I'm aware of. So, -- but in our assays, when we do these things, they are in single wells. So, we wouldn't see that. We don't run them as a large population in this case.

So, during rearing processes, just for rearing populations, they were usually in group containers, but I'm not sure. There might be somebody else better that can answer that question if they are cannibalistic or not. I'm not aware that they are.

DR. HELLMICH: Well, I just wondered if

you could have a high population and they could be feeding on each other and to that second or third instar and then survive. That's why I was asking.

DR. VAUGHN: My understanding of density dependence is it's resource limited. I'm not sure if they are actually using each other as the resource.

DR. HELLMICH: Would you explain to me how do you think they are grazing, what this grazing behavior is all about and contrast that with normal feeding behavior of a first instar.

DR. VAUGHN: Sure, Dr. John Foster has done a lot of this work -- he and his graduate student at the University of Nebraska. Obviously, work with corn rootworm is very difficult because of the location of the feeding.

So, we're not able to see this happen out in the field very easily. What Dr. Foster has done was created a medium where he can grow corn root in a test tube, essentially with an artificial matrix.

The corn plant is allowed to grow and it grows very well. Then they infest those test tubes with either eggs of corn rootworm or with larvae and he runs comparisons, side-by-side comparisons, looking at MON 863 versus isoline and then takes videos and captures frames of corn rootworm larval feeding behavior.

What he found was that if you look at a conventional hybrid growing in the system, the larva will trap the growing root tips through the CO2 that percolates through the soil matrix, finds the root tip, takes a bite and then starts to bore into the root and up through the root system.

It is not really clipping the root at this point, so maybe I need to come back to Dr. Andow's comment in just a second too.

In that case the insect bores up through the root and tunnels it out eventually, that root is back to the point where they stop feeding. With MON 863, what seems to happen is they located root tips identically.

But when they take that first bite they turn around and stop feeding and might stop feeding for many minutes, 12 to 15 minutes, and then they can turn around and they'll take another bite. But as they are doing this, they are moving from the location that they just took the previous bite.

So, they are moving around the root system, grazing on cells on the outside of the root itself. So, that grazing pattern is what is responsible for that root damage rating where roots are not clipped.

So, you see this grazing pattern, the roots are scarred, but you don't see large amounts the of root clipping.

DR. HELLMICH: Then what happens then they become later instars?

DR. VAUGHN: So, then later instars don't typically live within the root anyway, so it is the first through the second instar. After that most of these insects are grazing in the outside of the roots, moving up the root towards the base of the plant. That happens regardless, once they become a second or third instar on a transgenic or a non-transgenic plant. They are moving up the side of the root and once they become larger insects.

DR. HELLMICH: So, the only feed damage that have you identified that would be -- as Dave was saying -- unexpected, would be the tunneling or --

DR. VAUGHN: Right. But under high-pressure situations you can have enough of that scarring where roots do senicize (ph).

So, you can still end up with a root that might look like it had large corn rootworm pressures, but if you look at the root itself and really look into it, you don't see that tunnel if you can find roots that have not cenessed (ph) yet.

So, in the field you can dig roots and you can see what that the roots -- what they look like and you can rate them. If you take a closer look you can look at the root and see if there had been tunneling within the root system itself.

That usually happens in the first and

second instar, not older instars. Again, that's probably more difficult than a root damage rating for someone to identify a tunnel.

DR. PORTIER: Dr. Federici.

DR. FEDERICI: Going back to your bioassays, is that plant material or Bt toxin itself?

DR. VAUGHN: Bioassays?

DR. FEDERICI: Yes.

DR. VAUGHN: Yes, when you determine the LD50.

DR. VAUGHN: It's the Bt toxin.

DR. FEDERICI: Is that Bt toxin produced in Bt or ecoli?

DR. VAUGHN: Bt.

DR. FEDERICI: It is unusual. I have never heard of a case where you couldn't get an LD50, lets say, against a second or a third instar, where you have a reasonably equal or a low to moderate dose. I don't know of any situations.

That's a strange finding and I'm just

wondering whether it has something to do with the way protein was produced.

DR. VAUGHN: I can give you a little bit of insight there. This was touched on before with the bioassays. These plates that we used, the diet is so sensitive to any sort of contamination that the protein we use has to be extremely purified.

We end up running this through a number of digests in order to clean this protein up so that we remove any possible contamination from spores or anything else. In the process of doing that we end up lowering the concentration of the protein. It has a stock solution that we start off with and then when we put it in the diet again, we're diluting it by the volume of the diet, so by the time we get through this process, the amount of protein that we start with has been diluted quite a bit by the time we end up with the diet in the protein -- or with the protein in the diet.

But for example, the LC50s -- and again

this is in some of the documents that you have received, the LC50s for Cry3Bb against first instars is around 75 PPM.

The upper limits that we can get protein out of our cultures is around 300 PPM. By the time we go through the dilution process of getting it in, we're down maybe getting 200 PPM as our maximum concentration.

DR. FEDERICI: But you could reconcentrate the protein by labelization or something like that.

DR. VAUGHN: So we have not done that against second and third instars. So, what we're looking at though is the range of protein that we're testing is within the realm or the range of expression by the plants.

So, you saw some data and maybe you got the handout this morning of what the expression is in MON 863. In a root system it's highest expression is somewhere in that 60 PPM range.

So, going above 200 or 300 PPM, maybe we can cause some mortality in second and third instars, but doesn't seem to have a real impact on what questions we're trying to answer.

DR. FEDERICI: One last question. What is the economic thresh hold for --

DR. VAUGHN: For root damage rating?

DR. FEDERICI: Yes.

DR. VAUGHN: Again, NCR 46 --

DR. FEDERICI: Larvae per plant.

DR. VAUGHN: I think it is usually based on the root damage rating. I don't know about larvae per plant. Bruce might be able to better answer that one than me, but root damage rating economic thresholds are anywhere between 2.5 and 4 on the 1 to 6 scale.

DR. FEDERICI: I can understand -- I understand the rating, but I'm just wondering what kind of lava population do you to have to get that kind of damage?

DR. VAUGHN: So, in natural situations, again, Bruce or somebody else with some more background in natural populations than I can chime in here. But we infest, in our field trials, with up to 1600 eggs per foot of row.

So, we're looking at 18 to 1,000 eggs per plant and we're getting root damage ratings on our untreated checks in that case in the 4 to 5, sometimes 6s on those plants. So, 800 certainly could produce an economic thresh hold.

I think fewer then that could also produce an economic threshold and then you throw in the density curves on top of this and I think the number is probably somewhere between a few hundred and many hundred per plant to cause an economic threshold but the precise number I can't give you.

DR. PORTIER: Dr. Hubbard, did you have anything to add to that?

DR. HUBBARD: Well, the number of larvae, when you infest -- the number of insects that become established when you infest at that high dose is very low compared to -- I mean, if you sample the corn plant -- we infested -- we have three years of data of infesting 100, 200, 400, 800, 1600, 3200 eggs per plant, different densities of eggs.

The number of larvae that we recover from plants over time from egg hatch to they are mostly -- the most that we recover even when there is 3200 eggs, the highest average sample of larvae that we recovered is less than 200.

Now I'm not saying that we're recovering all the larva that became established on that plant, but there isn't a -- the majority of insects do not become established and grow into second instars, third instars and there is of mortality in the establishment process.

DR. FEDERICI: Just to clarify one thing, what instar pupation -- when you say you have 2 or 300 or 400, what instar would that be?

DR. HUBBARD: It is all the instars. I mean, initially, you probably recover more of the neonates at early egg, but until -- the number is high until you get to pupation. And then the way you recover is a behavioral way driven out by heat. So, when the insects start to pupate, our recovery is lower.

DR. PORTIER: Dr. Gould.

DR. GOULD: In a suggestion that comes from Dave and Rick's comment about the unusual nature of having tunneling on the MON 863 is that that could be used as a monitoring approach.

I was hearing that you were thinking maybe it would be difficult to use it as a monitoring approach?

DR. VAUGHN: Yes. I mean, if you think about it, if you take the number of insects that could survive on a given plant and you have that grazing that is intensified, what might look like clipped root or three or four or something like this, on a 1 to 6 scale, you wouldn't be able to say that that was because corn rootworm larvae were able to tunnel through.

It could just be excessive pressure and root damage from wounding from some other source that also caused that. You can have damage that looks like corn rootworm damage, caused by other factors, other insects and so it would be --

DR. GOULD: Could a researcher, though,

tell the difference or would that to hard to establish?

DR. VAUGHN: Very experienced, perhaps. I'm not sure. It would be a tough call.

DR. GOULD: I just wondered. Okay. Thank you.

DR. PORTIER: Dr. Caprio.

DR. CAPRIO: Ty, I just thought I would give you opportunity to respond here. Have you mentioned a lot about conservatism in the modeling that was used and Fred mentioned that as you vary dominance or as you vary different things, that the impact of refuges changes and certainly dominance is very important and I noticed in looking over Monsanto material is that you used a dominance of 1, which is rather unusual in that the times are very short.

But it does tend to make refuges appear much less effective than they might be if you chose other dominance values. Is there a reason why you chose that value of 1? It just seemed rather unusual to suddenly see that.

DR. VAUGHN: Yes. We actually looked at a range of levels and within that range of levels by varying dominance, the impact of refuge didn't matter as much on what happened to durability. So, we actually -- it is obviously a model that you can change the dominance level of.

I'm not exactly sure which model it is you are talking about in this specific case but within any of these we can change that dominance level.

Again it is not something that we have any precise estimate of what the value ought to be. If it is a single gene, it changes versus if it is a double gene, a polygenic situation. situation.

DR. CAPRIO: I have one other question, which is more thoughts about modeling.

When you talk about the first and second instars, the one that ones that have the different behavior and then trying to relate this back to the ten-day delay period, do you have any idea when -- does most of that delay occur as first or second instars or in other words, once you have gone -- once they have made it past second instar do they develop at pretty much the normal rate or do you have any knowledge of that?

DR. VAUGHN: Yes. We actually have done a little bit of work with that, trying to do some destructive sampling over time, trying to find what that curve of development looks like and where change occurs. What seems to happen -- I'll start with maybe some of the field insights that led to us this.

The first thing we do see is that under natural situations with no MON 863 involved, you typically end up with up with a 50-50 sex ratio. You can skew that by planting later. So, what happens is you end up with a female biased population if you plant later.

So, males are emerging first and they are feeding right and if there is no plant material out there for them, they suffer the highest levels of mortality. So, in that situation you end up with female biased sex ratio.

With MON 863 we see this delay in emergence.

We also see that same female bias sex ratio. So, it seems that the males, again, are suffering the highest levels of mortality.

So, what we have done is we've done a greenhouse assay where we can put single plants and infest with a known number of eggs and then sample over time based on what we think the development rate ought to be on a conventional hybrid.

Then we take that that soil from that pot and we start sifting through it to find all the insects that we can, counting as well as weighing them and giving them instars.

So, the curves differ the most between the first and second versus the second and third. So, most of that developmental delay seems to occur only on in the life cycle when they are first instars.

They are not able to get into that root, into the cortex of the root. Perhaps where there is higher nutrition, increased sugar content, whatever, they are feeding on suboptimal resources by feeding on the outside of the plant.

It is higher callus, it's higher ligament content, things like this, versus the inside of the cortex. So, I think that is probably what is causing this delay initially. That just follows through after they become second instars.

But again, that's very preliminary. I think there are some more studies that need to be done on that one. We have a bunch of those that are ongoing with Dr. Lance Mikey.

DR. PORTIER: Any other questions?

Dr. Neal.

DR. NEAL: Yes. In corn rootworm, you have a situation where a corn plant has a root system that can tolerate a certain amount of damage.

So, with your particular product, how much of the efficacy stems from actually eliminating larvae and how much efficacy comes from perhaps changing the feeding pattern of the larvae and the types of damage that they are doing to the plant?

DR. VAUGHN: There are a lot of -- there is a lot of information in that question.

I think -- let me take this in a couple of different pieces. There is a lot of environmental noise just in looking at adult emergence anyway.

Then, if you look at this across geographies, and what we know about survival of first instar larvae and different situations is that larvae -- first instar larvae in particular are very much prone to desiccation and other environmental factors as well as different soil types can cause increase in mortality.

If you look at the amount of survival and you look across geographies and then you throw in on top of that the environmental soil moisture or even drought in this case this past year, drought was a bigger factor. You can have a lot of pressure and really not see much damage.

In the case this summer -- this again was from Dr. Mikey in Nebraska, he had some dry land trials planted and serious draught conditions and he said he could go out and take a look at these plants and he could tell you which ones were protected by -- the plots, I'm sorry, and take a look and see which plots were protected by Cry3, just by the patterns of the leaf and how they were rolled up.

Those protected by Cry3Bb, the leaves were not rolled up. Those that were not had leaves that were rolled up. He was associating this with the amount of stress that the roots were actually under during that draught period.

So, those roots that have -- or those plants that are under those serious drought conditions might end up with a lot more damage than you would expect if they were not so stressed from drought or other conditions. I'm not sure if I got to the second part of your question though.

Could you have -- maybe if you could repeat that again?

DR. NEAL: Well, how much of the efficacy of your product is due to changing the pattern of insect feeding and how much of it is due to actually causing mortality?

DR. VAUGHN: I think the majority of it is caused by changing the insect feeding pattern.

I think because of the -- that 20 to 60 percent mortality that we see or what we're calling mortality, because of the adult emergence patterns compared to the untreated checks, there is some range in there where you could cause as much as 20 or as much as 40 percent mortality.

But, again, the feeding pattern -- the root is protected because of the feeding pattern. So, there is some portion of the population that is called out initially, probably some males initially, and then you end up with female and some male damage after that, but you do have some impact on if initial population with mortality. It's not that they are all still around.

We do have excellent efficacy on these plants. It's just that the kind of damage they are creating is not economic at this point.

DR. NEAL: If you did have a population

that developed resistance so that they were causing economic damage to the transgenic plant, what would the characteristics of those individuals be?

DR. VAUGHN: I think the way that we have looked at this, and I think the plan for other transgenic crops is a good model to use. You would be looking for things like changes in the level of tolerance from those populations. You would be running that dose response curve looking for changes in the LC or LD50s and looking for changes in the slopes of those values.

Beyond that then we would be verifying that the plants are the plants that we know there is meant to be in the field. And then we would be looking at whether or not -- what kind of damage we get on those plants under controlled conditions.

So, putting populations that came through our bioassay back onto plants within a greenhouse and taking a look at the kind of -- or the levels of damage that we see.

I think those would be the two phenotypes that we would be -- other than that, I think you are hard pressed to and find a phenotype. You have to look at damage or susceptibility.

Susceptibility seems to be something we do have enough information on and ability to do at this point.

DR. NEAL: Is there any correlation between planting time relative to rootworm emergence and efficacy?

DR. VAUGHN: Sure. You can plant early enough so that the plants are out of the ground and the root system is well enough established that you just don't end up with as much damage.

So, you've pretty much -- you have planted ahead of the emergence pattern of corn rootworm or you can plant late enough so there are no corn rootworm larvae actively feeding when did you do this.

Those haven't been very widely used strategies, because growers aren't willing to take the chance that the weather is going to be okay three weeks from now just to prevent some corn rootworm damage to their fields. Typically, the -- I think we heard this morning too, there is a pretty tight window of time have to get this these fields planted. So, delaying planting isn't really an option. It can -- it could definitely change the amount of damage you experience if you did that in any given field. But again, that's stochastic as well, unless you scouted the year before.

DR. PORTIER: Dr. Hubbard.

DR. HUBBARD: One quick comment and also, a quick question.

I think we want to be careful in looking for quick fixes, such as like tunneling, as a tool for monitoring for resistance.

My experience has been closer to Dr. Tollefson's in that the amount of damage from the MON 863 and the five years I have been looking at it, has been maybe forty-fold less than my untreated check, like a 1.6 to a .03 or something like that. That's fairly typical of what I have experienced.

The very same study are you referring to from Lance Mickey, this summer where they had very dry conditions, very heavy pressure and the roots don't recover well under heavy pressure and drought.

They had some floor damage, I mean a full node of roots on some MON 863 expressing plants that was verified. I would say that those roots were probably tunneled if they got -- node roots that were destroyed.

Under those extreme conditions, I would have called that unexpected before hearing that from Lance, but I seriously doubt that that is resistance. I think we want to be careful and probably actually looking at the baseline LDC 50 versus tunneling versus scarring around the root. That's a comment -- quick question.

You refer to your laboratory -- your greenhouse studies, your single-pot studies -- it is in your mitigation, I couldn't find it, but you refer to controlled greenhouse studies. How many larvae are you testing per pot in those controls?

DR. VAUGHN: Typically, in efficacy trials, we use between 800 and 1,000.

DR. HUBBARD: In one pot?

So, you destroy controls and --

DR. VAUGHN: The controls are typically fives and sixes.

So, just to follow-up on that comment, that is kind of where I was going with what David was talking. You can get that kind of damage for other reasons.

So, environmental conditions, soil types, things like this can cause what look like -- and maybe it is tunnelling at some point but it is probably very different than what you would typically see.

So you can get higher levels of damage depending on the kinds of environmental conditions that you are under. If the plants are seriously stressed the plants are going to look much different than those that are under controlled conditions. So, good point.

DR. PORTIER: We have had Dr. Vaughan on the stand here for almost an hour. I'm going to ask that we sort of try to end up with our questions and keep our commentary for the discussion of the EPA questions in a moment.

Dr. Whalon.

DR. WHALON: I would just like to go back to the comment that John Tollefson made about asynchronous sentinel fields as a monitoring strategy.

Did you guys think about that? How do you react to that in this setting?

DR. VAUGHN: I think it is something we could definitely try and see how it works.

I guess in my mind, I haven't thought through it completely yet and maybe John has -- is how do you go about doing that?

Does each grower provide a sentinel field, is it something that is more cooperative in a region? Do -- did someone set aside some acreage? Whatever you set aside is going to essentially going to be completely prone to whatever insect pressure there is.

So, someone is going to be willing to take that acreage and take it out of their production, but yet they have to go ahead and pay for it and plant it and keep up the agronomic practices on that acreage, whatever it is.

I think there a lot of work that needs to be thought through before that is -- something like that could be implemented.

DR. WHALON: How about applying it as a mitigation strategy in a situation where you have observed damage?

DR. VAUGHN: That would be -- to me, a sentinel plot would be a great way to collect additional beetles from areas where some reports have come in or something like this.

Yes, I think in a mitigation strategy you could put up a sentinel plot and try and collect beetles and then get those into our bioassays as fast as possible. That way we would have enough beetles to actually work with to get decent dose response information out of it.

DR. WHALON: Finally, area -- restricted areas based on worst case scenarios, corn-on-corn-on-corn, very intense. We talk about that, think about that.

What is your reaction to that? It is another concept we discussed with Dr. Tollefson.

DR. VAUGHN: So, areas where corn is -- so corn-on-corn-on-corn for many years? So, just -- you are talking about just increasing the selection pressure with --

DR. WHALON: Essentially, yes.

DR. VAUGHN: So, again, because the plan has built within it a structured refuge within a distance that beetles will be encouraged to mate with one another, that is why the refuge is there to begin with.

So, under the worst case situation, under the highest pressure available, you would be looking at selection on plants. That's what happens.

DR. WHALON: But under your own comment,

you seem to suggest that 20 percent refuge doesn't really matter.

I'm just trying to build in another safety feature maybe that would do something.

DR. VAUGHN: No. So, not that it doesn't matter, it is the relative impact of changing it from 10 to 20 to 30 doesn't have much impact on durability overall.

We haven't -- so, again, you are going to be looking at precise estimates within a model to understand what that looks like. At least to this point, the true characteristics of MON 863 have not -- those parameters have only recently been put into some of these models.

I think there is value in doing that, but under the worst case situation, I think that's what we're trying to do with the models. This is worst case. These are areas that are 100 percent adopted. We know what this looks like.

Here was the outcome based on levels of refuge that we put into the model and the amount of refuge just didn't change the overall outcome that much. So, not that it is unimportant. Right now we believe it is and that is part of the plan.

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: I have a quick question.

I understand that this Bt product will not be stacked with the corn bore product; is that true, at least presently?

DR. VAUGHN: At least right now we're putting some packages together.

That's what growers would really like to have, is something that would -- in areas like David was talking about, they have two pests to control, corn bore and corn rootworm. Making them choose between them essentially limits the adoption of one or the other.

So, you are causing that. So, at some point, yes. I mean the idea is to have corn bore and corn rootworm traits together.

DR. HELLMICH: What about the roundup ready trait?

DR. VAUGHN: Again -- so now we're getting out of the range of a technical person like me, but I think the plan is to have products available meet grower needs within specific regions.

DR. HELLMICH: But right now they won't be stacked with anything; is that true?

DR. VAUGHN: Again, I'm going let Dennis, maybe -- we've applied for registration for the stack. So, that's an ongoing process with the EPA right now.

DR. HELLMICH: We don't have to consider that in this panel?

DR. PORTIER: Right.

Last comment, Dr.Weiss -- last question.

DR. WEISS: I would like to go back and get my computer and come up here.

Has it been the experience of Monsanto that whenever you use this event you get a -- under field conditions you get askew toward female emergence?

DR. VAUGHN: Where we have looked at this with adult emergence cages, yes.

DR. WEISS: So, if you ever got a field

situation where you got a 50-50 sex ratio or more skewed toward males, would that be an indication that you have a problem with resistance or something like that?

DR. VAUGHN: So,I think this gets even a little more confusing it would depend probably on the planting date as well. DR. WEISS: if you planted later, you would get it all askew toward females anyway. So, if you planted traditionally or early, you would tend to get 50 percent sex ratio. But if you -- so, if you planted late, even if it was a MON event, you would still see a lot of females.

DR. VAUGHN: I think that that would be the case if you had a side-by-side comparison. You could end up planting it whatever tradition is for any given grower, you could still end up hitting the curve of optimal emergence or you could be on either tail of that curve.

So, I think you -- the only way that would work is if you had side-by-side comparisons perhaps. So, you would see what the natural situation is and then you could compare that to a MON 863 field.

DR. WEISS: Okay. I'll let it go.

DR. PORTIER: Dr. Andersen, Ms. Rose, any questions, comments?

DR. ANDERSEN: I think we're fine, thank you.

DR. PORTIER: Dr. Vaughan, thank you very much.

DR. VAUGHN: Thank you, again.

DR. PORTIER: Are there any other public comments from individuals who have not had an opportunity to comment as of yet and would wish to make a comment?

Seeing nobody raising a hand or standing up, I'm going to close the public comment section and we'll begin now with the first question from EPA.

You better read a bit of the preamble to this.

MS. ROSE: Do you want me to read the entire preamble also?

DR. PORTIER: Just the part that starts with "The panel has requested."

MS. ROSE: Okay. I was going to do that. Thank you.

The first question relating to pest biology has four parts to it. "The panel has requested to comment on the Agency's conclusion that additional information is needed on various aspects of corn rootworm pest biology as it relates to long-term IRM strategy.

Specifically, discus whether an IRM strategy designed for western corn rootworm and northern corn rootworm is applicable to other corn rootworm species.

How much species specific data is needed versus how much can the Agency rely on existing data that for western and northern corn rootworm to predict what would be about an adequate IRM plan for southern and Mexican corn rootworm."

DR. PORTIER: Dr. Weiss.

DR. WEISS: I think the question needs to be kind of divided into it's component parts.

We could start the discussion with the first part --

DR. PORTIER: Could you get a little closer to the microphone for us, please?

DR. WEISS: Oh, I'm sorry.

Fred's rubbing off on me here.

I think we need to divide this part into the more specific questions, whether the resistance management strategy designed for both the western and northern is applicable to other is a broader question.

I think if we could go down to how much species specific data do we need on the other two species, primarily the Mexican and the southern as it relates to this management strategy proposed for essentially the western and northern corn rootworm.

DR. WEISS: Dave just asked me what is my answer.

My opinion on this, based on what I have read is for the southern corn rootworm we do know that it has a wide host range -- over 250 hosts.

In the central corn belt, I would consider southern corn rootworm a very minor corn pest. It has been my experience that it tends to show up on late planted corn, but other than that, it is a very minor corn pest.

So, with a huge host range, it seems to me the insect is already built-in a rather large internal refuge by having such a wide host range unlike the western and northern, which is very specific to corn.

It seems to me the selection pressure for the southern would be very minimal -- would be the point I would throw to the panel to discuss.

DR. PORTIER: On the Mexican?

DR. WEISS: On the Mexican, my understanding of the distribution -- geographic distribution of this pest -- it's limited mainly to Texas and Oklahoma.

Bruce, is that correct, Oklahoma is in there too?

DR. HUBBARD: I think so. Kansas, too.

DR. WEISS: And Kansas?

To me, although Mexican corn rootworm is very similar in appearance to the western, I don't know if we really know enough about its dispersal patterns, particularly adult dispersal patterns, to answer that question now.

DR. PORTIER: Dr. Hubbard.

DR. HUBBARD: The Mexican and western corn rootworm are subspecies, so they are not different species, they are in the same -- they are defined as "Subspecies." The western corn rootworm -- diabrotica virgifera virgifera are the westerns. The Mexican diabrotica virgiferazea. Much of the data generated for the western corn rootworm may be applicable to the Mexican corn rootworm, but should be verified when practical.

Types of data that are most likely to be different would be behavioral data such as adult movement because even within the western corn rootworm biotypes from Nebraska and Illinois are vastly different when you are talking about adult movement patterns.

During the interim period in more come

complete data sets of transgenic efficacy and adult emergence from transgenic corn for both the Mexican corn rootworm and the northern corn rootworm -- I think would be useful.

The southern corn rootworm in the same genes, but as Dr. Weiss mentioned, they are very different in their biology. Information on the western corn rootworm is less likely to be applicable to the southern corn rootworm.

Although, as we heard earlier, -- although -- we didn't hear this completely -- neonate western corn rootworm, Mexican corn rootworm, northern corn rootworm and southern corn rootworm are all controlled with similar doses of Cry3Bb1, Monsanto's product, as I understand it.

But in their -- in Monsanto's reaction to this question, they state that the southern corn rootworm is not adequately controlled by MON 863 under field conditions. That's probably because the biology of the southern corn rootworm, unlike western corn rootworm where eggs over-winter in the soil, the southern corn rootworm eggs are laid by overwintering adults and rarely, if ever over southern adults rarely over-winter in most of the corn belt, although I think they occasionally do as far north as Columbia, Missouri. In early spring, adults lay eggs near grass.

Southern corn rootworm eggs may hatch before corn roots are available and feeding on grassy weeds before movement onto corn roots when they become available.

So, larger instar southern corn rootworms as well as larger instar western corn rootworms are not controlled by MON 863, as Ty mentioned earlier.

But since Monsanto does not claim that their product controls southern corn rootworm in the field, I think southern corn rootworm should just be removed from the label.

DR. PORTIER: Any other comments from the panel, disagreements, agreement?

Dr. Gould.

DR. GOULD: Just on the question itself, it asks if we can rely on --

DR. PORTIER: Please use the microphone.

DR. GOULD: If we can rely on existing data for western corn rootworm and northern to corn rootworm to predict what would be an adequate IRM plan for southern and Mexican, and I think it brings back the question of -- do we think we have enough existing data on the western northern to even develop an adequate IRM plan for those species themselves?

So, I mean, if there are two things imbedded in that question.

I don't necessarily want to get at it right here as to what we think of that first part of the question, but I think it should be mentioned. That's all.

DR. PORTIER: In other words, what you are saying, Dr. Gould, is that the answers we have given are conditional upon believing the IRM for the western and the northern, are, in fact, adequate.

DR. GOULD: Exactly, yes.

DR. PORTIER: Since we haven't discussed that yet, any other comments or answers for this question from the panel? So, if I can summarize our answers we have sort of got two different things from the panel so far for the southern corn rootworm, that the IRM is likely either not to be needed or in fact it should just be removed from the label for efficacy reasons as not being controlled, in which case the IRM is not needed either.

The Mexican corn rootworm on the other hand, not enough is known to be able to answer this question, but the western corn rootworm results should apply and they should be verified especially in the case of the adult movement.

Have a caught the salient features here?

DR. HUBBARD: Yes. We just don't know whether it is going to apply, but they are in the same species and certain types of data are likely to be applicable, others types of data are not, and behavior of adults is probably -- I don't know anything about Mexican corn rootworm adults, I haven't worked with them, but I would expect they would be different.

DR. PORTIER: Dr. Neal, did you want to pitch in on this? Dr. Neal, did you have something to add for a minute? No?

Okay. I think that ends part A, we'll go to part B.

MS. ROSE: The panel has asked to discuss whether and, if so, what additional research regarding male and female adult and larval western and northern corn rootworm dispersal potential is needed to determine placement of non Bt corn refuges.

DR. PORTIER: Let's reverse the order this time.

Dr. Hubbard.

DR. HUBBARD: The response of NCR 46 to a similar question in May of 2001 was as follows -- continue to quantify movement patterns of corn rootworm larvae when feeding on transgenic expressing Cry3Bb and nontransgenic corn.

Quantified pre and post mating dispersal of corn rootworm movement with -- between fields and its implications to the corn rootworm for IRM.

Evaluate IRM options other than a refuge strategy, especially if the event is not classified as high dose.

Examine the impacts of refuge configuration including seed mixtures on development of resistance and the likelihood of farmer adaption.

Evaluate IRM options other than a refuge strategy, especially -- I guess I repeated that.

Many of these studies have been conducted or initiated since the time of that letter in May 2001. One of the things that is probably the most needed now is large field studies to understand how the expression of Cry3Bb one, in above ground tissues affects adult movement and, I guess, mating patterns would go into the next question.

When possible, additional data on many aspects of the biology of the northern corn rootworm and Mexican corn rootworm should be collected. But it is not -- unfortunately, many of these studies -- many studies done with the western corn rootworm may not be physically possible with the Mexican corn rootworm or the northern corn rootworm because rearing is very difficult. There aren't necessarily experts to be able to do this in the areas that these insects are present.

That's all I have for now.

DR. PORTIER: Dr. Weiss.

DR. WEISS: I think according to what we heard today from John Tollefson and what has been included in the material that has been provided to us, relatively speaking, I think we know quite a bit about western corn rootworm female movement and migration.

The question that I have in my mind is, the male migration in movement and how does that occur and how frequently does that occur and how are does that occur?

I think with -- I agree with Dr. Hubbard that what we know about northern corn rootworm female and male movement and Mexican corn rootworm male and female movement is extremely limited when you compare it to western corn rootworm, what we know about western corn rootworm.

I think the -- in my mind, I am more concerned that we understand and have a good understanding of adult migration than larval migration, particularly if the refuge plan is outside of a cornfield that has the event in it. If we go with blocks outside of an existing cornfield, I think larval migration is a moot point.

DR. PORTIER: Any other comments from the panel, disagreements, different aspects?

Dr. Hellmich.

DR. HELLMICH: I have a question.

I know that Joe Spencer, from the University of Illinois, has been working on movement -- rootworm movement for a few years now. Is there anybody in this room that is familiar with what he is doing and how it may give us some information that we could put in here?

DR. HUBBARD: What specifics are you interested in?

DR. HELLMICH: Well, I have seen Joe gives talks. He talks about thousands of root worm beetles moving out of fields and he is trying to -- trying to capture them in these nets on top of these big stands. I think he is crazy because he is going to fall off one of those one of these days, but at least his data suggests there is a lot of movement.

It is, for example, it's unfortunate we don't have any kind of summaries of what he has done. The data from Illinois and John Neal may answer for Indiana insects which are similar

DR. PORTIER: Dr. Hubbard.

DR. HUBBARD: John Neal may answer for Indian that insects, which are similar patterns, probably. So, there is a great deal of movement back and forth between fields, as I understand listening to Joe's talks in the past.

Just the biomass that is in the air at a given time from this past year -- just were astronomical figures, talking about flocks of Canadian geese per hour or something like that.

The movement patterns in other areas such as Iowa and Nebraska, I think, are greatly different. And so it is not only species specific, but it is location specific.

DR. NEAL: I would like to reiterate that possibility that the movement of male and female adult western corn rootworm may be very different in the western part of the range than the eastern part.

DR. PORTIER: Other comments?

Dr. Gould and then Dr. Andow.

DR. GOULD: One comment is that reading the literature, there are studies but they are very few, so it could even be not only regional, but just happen to be that year and when it was studied from the way it looks from the literature.

The other comment is, of course, if you have this resistant corn in those areas, you are going to change the densities. I think the comment was made that we need an understanding of how density is affecting that movement. I think it was mentioned before but I would like to restate that.

DR. PORTIER: Dr. Gould, then in terms of the types of research we might need, would you say then multi-year research in the same area is something that would be important here since there may be a temporal affect?

DR. GOULD: Yes. I think definitely, you would need that and different densities. I'm not sure just what EPA wants from us in terms of how much detail they want us to give them in terms of how these studies should be carried out. It would be helpful to have a comment if possible from EPA.

DR. PORTIER: Dr. Anderson, Ms. Rose?

DR. ANDERSON: Well, first let me go back to the question about the Spencer's (ph) work.

We actually do have in this room a study that was submitted to the Agency regarding -- as part of the experimental use permit package, which if you would like to do little evening reading we would be glad to provide it to the SAP to provide a copy to all the members of the panel if they would like to see it.

It's a publicly available study but one we did not submit to the -- actually, to the panel. We haven't given you all the research data there is just because it would be pretty hard to give read it all in the time frame we have given you. But that particular study, any member who would like to have it, we could do that.

Give me a guess, Robyn, how long it is? Preliminary study, so we'd be glad to do that if you'd like to see that.

DR. PORTIER: I'll answer for the panel and you should just go ahead and give it to us and if there are additional comments tomorrow at the very end of all the questions, we can always ask the panel to come back.

If they have additional comments on all your questions, we can add it in.

DR. ANDERSEN: That would be great. Now, I'm going to let Robyn More respond but we were leaking at the study a bit. If you wouldn't mind, Dr. Gold, to just repeat a little bit of what are you actually asking for us?

DR. GOULD: I think it was good that you, Chris, brought up this question of -- well, am I saying that we need repeated studies, a multi-year in the same location? I guess, what I'm trying to get at is what kind of detail do you want us to indicate?

Do you want us to indicate there we think there are density dependent studies that need to be done or do you want us to give you more detail in terms of what would be sufficient.

I think some of the things that have come back in the past is that you don't get enough detail from us. I'm not sure what level you are looking for.

MS. ROSE: I would have to say the more detailed the better.

DR. GOULD: So, if we gave you almost an

experimental -- a very brief experimental design that would be --

MS. ROSE: Yes, actually.

DR. PORTIER: Dr. Andow.

DR. ANDOW: No experimental design from here, but just to reiterate -- in terms of what I think we need to know about movement is, I think we need to know average movement rates and that includes distance per time and leaving rates from the natal fields, the fields they are born in -- of the males and mated females of the western and northern corn rootworms since we're focusing on them.

To some extent having some information about the mated female movement of the westerns helps because we can sort of look at the movement of some of the others relative to that.

In addition, this issue of density dependence of movement, I am particularly -- feel it is particularly important to know whether male movement is density dependent, because most of our analysis of these resistance models suggests that it is male movement -- lets see, I have a little diagram here of that -- it's the effect of the different movements of the females and males from the Bt or the non Bt field have very different affects on resistance evolution rates.

And that in general, movement of mated females from the Bt field to the non Bt fields accelerates the rate of resistance evolution and movement of males from the non Bt field to the Bt fields delays the rate of resistance evolution. Those are two of the major factors we found in terms of how movement interacts.

So, in terms of understanding how the delays occur, it would be very important to understand how the males respond to the Bt versus the non Bt which relates to the toxin in the fields as well as the densities between them. So, that's on the delay side.

On the bad side, it is the females and knowing to what extent they are repelled out of the Bt field or -- either because it's low density or because of the toxin.

So, those are two things on the movement. And then in terms of larva movement, I guess, given what we're understanding about the feeding behavior, it seems that if we even want to consider mixed seed refuges, the main question is in my mind is do the first instar larvae frequently move from Bt plants to neighboring non Bt plants. DR. HUBBARD: I have two years of -- well, I started the second year of study on that very question and I can answer it here if you desire to -- whatever.

DR. PORTIER: Bruce Hubbard, do you wish comment on the affects of Bt corn on -- How about a recommendation?

DR. HUBBARD: A recommendation?

DR. PORTIER: In terms of how you would design such a study to address the question or does it need to be addressed if your research is has already addressed it.

DR. HUBBARD: I think I have already addressed it with at least one soil-type -- or after this years's data is collected and analyzed.

DR. PORTIER: So, are you suggesting that it needs to be done on other soil types or are you suggesting --

DR. HUBBARD: I'm not saying that one study in one location in Central Missouri is going to be applicable for all -- for other soil-types for sure. I can't answer that, but the likelihood is high.

DR. PORTIER: Dr. Hubbard, what did you find?

DR. HUBBARD: Well, there is a number of possible impacts of transgenic corn on larval behavior.

One, I had an infested central plant surrounded by uninfested neighboring plants. That infested central plant was either MON 863 or an isoline.

It was either surrounded by -- an isoline surrounded by MON 863 -- MON 863 surrounded by isoline or straight isoline or straight MON 863.

We infested the central plant. We

collected -- we sampled the central plant and plants down the row and across the row over time. We found no evidence.

The number of larvae recovered from the neighboring plant, which was isoline -- when MON 863 was infested was not significantly higher than when they were all isoline.

In other words, they did not take a bite of MON 863 and move to the neighboring plants before receiving a lethal dose.

When isoline was surrounded by MON 863, the number of larvae that were recovered on MON 863, the neighboring plants was actually zero.

In other words, they prefer to stay on the infested isoline plant and did not migrate to the nearby MON 863 plant and it was significantly lower than the number recovered on those neighboring plants when it was straight isoline. It appeared to be slightly repellant or more toxic than to second and third instar larvae than reported today.

They did -- although I did not recover

larvae on that 863 plant, once that infested the isoline plant received a very high level of damage -- basically two nodes of roots completely destroyed, larvae did move -- well, significant damage did occur to the MON 863 neighboring plants even though I didn't recover larvae.

It was probably right before pupation significant damage to MON 863 did cur occur.

DR. PORTIER: Any other comments on this question Dr. Gould?

DR. GOULD: I just want to make a cautionary comment. I would like feedback from other people who have been modeling. I have been trying to going through these models for the last few days.

One of the things I do think is important is get this movement data on the males and the females. There is the issue of how important is the pre-mating -- the movement of the males before females mate and such.

I think we always keep our mind set, because of the original work on resistance management, looking at a high dose is assuming there is recessiveness, a nonadditive inheritance.

But, with this kind of a low dose or moderate dose effect, there is no real reason to assume recessiveness and if have you an additive model, then the mating structure to everything I have seen doesn't matter much at all.

I would like to set that out as a challenge. Maybe we do not need those kinds of studies on the impacts of mate movement of males before the females are mated.

I would like to hear feedback on that, because, if we're going to make that suggestion, we better be sure it is important.

DR. PORTIER: Dr. Caprio.

DR. CAPRIO: I'll just back that up with some of the data that I was going present later that pre-mating isolation had very little impact under these sorts of scenarios.

Some of dispersal related to our position did have a large impact but not pre-mating isolation.

DR. GOULD: Under the moderate dose?

DR. CAPRIO: Under moderate dose, yes.

DR. GOULD: So, do you think that we don't need those kind of studies then? I mean, I think is we are going to suggest something to Monsanto, I think we should -- DR. CAPRIO: I think they are less important.

DR. GOULD: Less important? Okay.

DR. PORTIER: We're suggesting to it EPA.

Dr. Caprio, under the scenarios you are discussing here, are all of those with a fairly rare recessive?

DR. CAPRIO: 10 to the minus 3 and 30 percent survivorship of susceptibles and anywhere from 35 to 45 percent survivorship -- heterozygotes.

So, I will still assuming some recessiveness, for those sorts of simulations, but it was -- there was almost no impact of pre-mating isolation.

DR. PORTIER: So, just to satisfy my own curiosity on this issue, is the panel fairly convinced that there isn't a high percentage of recessives and that the low mortality you are seeing from the Bt crop is due to a large protected population?

Did i make that clear?

MR. VOICE: Repeat that, please.

DR. PORTIER: If I were talking in terms of larger animals, the mammals I work with, we would be talking about genetic polymorphisms, which come in any percentage that you care to have them.

Since we haven't applied this particular crop management tool yet, we don't honestly know whether there isn't a protected population governed by some genetic polymorphism that is actually high prevalence, not low prevalence.

If there is selected pressure against the 20 percent protected population, what would be the impact? But if you don't believe there is any chance of a large protected population, then it doesn't matter.

Dr. Caprio.

DR. CAPRIO: I guess I would just say, if the resistant trait is present at 20 percent frequency, there is almost not a product to protect -- at that point there is nothing you can do.

I think assuming some sort of assuming some sort of rarity to that resistant gene is just a prerequisite to even attempting a management resistance.

DR. HELLMICH: The question I have for Fred and Mike, then, is under these conditions, do we really need the larval movement research?

DR. PORTIER; I'm seeing a yes, from Dr. Gold for the record.

DR. GOULD: For the record I would say that they are not that important because of that same reason.

I'm not going to say they couldn't be important but we can't -- you have to make a lot of assumptions about the genetics and the feeding behavior for that to actually be that important.

DR. CAPRIO: I can't comment on the larval issue with a low dose or moderate dose. I have not done that.

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: One other time I made this comment in public and Fred -- I had a great reaction from Fred, so keep your eyes on him this time.

Does that mean that perhaps seed mixtures would be a possibility in this case?

DR. PORTIER: Dr. Gould.

DR. GOULD: Yes; it does. I think that the models that I have seen indicate that none of them will give you good resistance management.

So, you know what I'm saying?

I mean, you could do it, but I think the problem is, I think, we had to have this gold standard of a high dose and now, we're talking about registering a product that is not what the -- SAP 1998 indicated that we should never register a product like this and now we're registering a product -- talking about registering like this and then we're asking these kinds of questions.

Well, the whole idea of not having a mixture was to get resistance management that on Nick's scale would be like tenfold or fifty-fold advantage. Here we're talking about one and a half-fold more time or 1.2 or whatever. It might have that kind of an impact, having a mixed seed might change it from 1.2 to 1.4.

I'm talking off the cuff here, but it is not going to have this major impact. It depends on how fine tuned you are looking.

DR. PORTIER: If I understand what we're saying -- what is going on here, is that the adult movement -- if any studies are done, the adult movement is more important than the larval movement. That's the consensus from the panel? Is there any distention of that? No.

Dr. Hubbard.

DR. HUBBARD: I would like to react to that last comment of Dr. Gould's in that this product -- it provides much more consistent protection than the soil insecticides that are currently available.

And it also provides less damage than the insecticides that are currently available. So, I think it is fully worthy of consideration.

DR. PORTIER: I will note that this Science Advisory Panel is, in fact, not registering this product or even considering it for registration. We are considering the scientific evidence necessary to look at insect resistance management on this issue.

It is EPA that is considering registration.

Dr. Caprio.

DR. CAPRIO: It occurs to me that when we originally looked at cotton, Fred was one of the people that really pushed for a low-dose strategy. One of the reasons it was not accepted for cotton were sublethal affects.

I think maybe, as Fred says, maybe it is time to take a look at some of those question, the reasons why a low-dose approach was originally rejected for the high-dose approach and whether or not we're going to see these same sort of sublethal affects. So, maybe it is appropriate to go back and remind Fred of his original position. I think to some degree these points are parts of the further questions we're going to come with in terms of the insect resistant management scheme.

So, I'm not sure we need to continue this discussion at this point. It is certainly going to come into something else and we're going to talk about in a little.

Dr. Andow.

DR. ANDOW: I have to ask both Fred and Mike to explain to me a little bit more about what it is that they think they don't need information on and why in terms of the mating structure issue of adults.

DR. PORTIER: Dr. Caprio.

DR. CAPRIO: Again, this is in a little pamphlet or whatever.

What I found with the model that I

looked at is pre-mating isolation had very little impact. We're talking about -- per various assumptions -- well, it was 56 with complete random mating.

DR. ANDOW: What do you mean by pre-mating isolation?

DR. CAPRIO: This is mating -- or dispersal prior to mating. So, movement in this two-patch model, prior to mating.

DR. ANDOW: So, isolation is no movement before mating?

DR. CAPRIO: Complete isolation would be --

DR. PORTIER: I'm sorry, Dr. Andow, I don't think anyone heard your comment.

DR. ANDOW: I'm trying to get an explanation.

DR. PORTIER: We can't understand the explanation if we don't understand your question.

DR. ANDOW: I'm sorry. The question -- we're going to share this -- the question is: isolation means there is no movement --

DR. CAPRIO: Correct.

DR. ANDOW: -- before mating?

DR. CAPRIO: Right.

So, with complete random mating, under the particular assumptions here -- and this is with a 50-percent refuge -- was 56 generations and if you had complete isolation -- no movement prior to mating it was 55 generations.

DR. ANDOW: That's contrasted with random movement then?

DR. CAPRIO: Yes.

Now what was what was different is movement after they mated but prior to oviposition and if you change that to say, 10 percent, so you -- so, if you have this pre-mating isolation or limitation on pre-mating dispersal, but if you have random movement before they oviposit, it may -- that's the numbers that I was talking about -- if you then limit dispersal prior to laying eggs, that number -- if it went down to 10 percent -- so, if we take John's figure of 15 percent, which I assume would sort of fall in that range, the numbers jumped up to 4,000 generations.

So, there is something very important about adult dispersal. I hesitate -- I should point out with that, there is no density dependence.

So, what is happening in the models, there is a huge population building up in this refuge which might be an isolated field and no grower would tolerate that sort of damage.

So, it is unrealistic in that sense, but it does say that you could buildup large populations in refuges and that those could significantly impact the time to resistance and there are very important parameters with adult movement, but I don't think it is prior to mating -- from my own model.

I think there is lots of different ways you model that and different questions that can come out of that.

DR. ANDOW: I would just like to say that our experience in the modeling business has been that when you actually have the density dependence, and so you actually do create some population dynamics, that then the mating structure starts to matter more.

It is because the -- it affects the numbers of individuals especially in these lower-dose cases, it affects the numbers that are coming off of the different places.

So, I would be hesitant to go along with that overall recommendation at this point.

DR. CAPRIO: I'll just say that those results are consistent across another model that does the same -- not for this species.

So, obviously there is different things that are going on I think it depends on when you have the density -- I'm not sure, honestly.

DR. ANDOW: It also depends on whether or not the model sort of makes the densities to come to some equilibrium fairly quickly and stay at that equilibrium.

DR. PORTIER: So, if the two of you, now that you have had this great discussion could characterize for us what data needs would you want to be able to separate the differences between the two models to get a better prediction which pertains to the question being the research that would be needed.

DR. ANDOW: I guess the way I was looking at it is that when you have a variable population dynamic, that you do need information about the movement rates, both pre- and post-mating in order to get a reasonable projection of the evolutionary dynamic.

What Mike, I think, was saying in his case where he either -- I can't characterize the models, but in his case there is not a need for that level of resolution on movement.

DR. CAPRIO: I would say there is for post-mating, but given the large survivorship of susceptibles, it doesn't appear as though that pre-mating -- in other words that pre-mating isolation can be important under other scenarios where there is a high dose. But it seems -- the way I try to explain it to myself it seems like there is enough susceptibles emerging even in these transgenic fields and enough movement of males and so on that it -- as limited as the results are -- I might not emphasize pre-mating dispersal, but I do think that post-mating dispersal -- there is still a reason to study adult dispersal.

DR. PORTIER: Dr. Gould.

DR. GOULD: I wouldn't say there is no reason, but I think in terms of trying to prioritize, I would put it lower.

The point I was making has to do with more straightforward genetics of, if you assume that it was additive, that each allele contributes equally -- each resistance allele contributes equally, there is no dominance affect, then mating structure really has very little effect in models, whereas when you are dealing with a high dose and you are assuming recessivity, then it really have a very major affect.

So, when we were talking high does, that was the key -- was to understand pre-mating movement and now, it is really not.

DR. ANDOW: I don't disagree with that assessment.

I guess the question is, are we really dealing with near additive case?

It seems to me that one doesn't want to jump completely into that boat at this point without knowing whether or not we have any evidence for that. You are definitely right, it could be that.

DR. PORTIER: Dr. Hubbard, did you have -- I noticed were putting your hand up there.

DR. HUBBARD: Just in this in question C, following this, there are a number of studies that are under way. I think it's unfortunate that this particular panel doesn't have additional members from NCR 46 on it, because this question was on the biology of the insect.

There are -- there is some expertise in the audience. I'm not sure at some point we may wish to consider bringing some of that expertise in if it were possible to see if there's -- I don't know for this specific question, but other questions there is expertise in the audience beyond the panel as well if that were possible for them to comment.

DR. PORTIER: Well, I'll leave that up to the panel to decide when they think I should invite someone else into hear.

Any new points on question B?

Dr. Whalon.

DR. WHALON: Just an observation.

Given where I was when I showed up this morning, I thought that there were classical doses mortality events going on here. After some of the comments we've heard from expert testimony from Monsanto in particular, it strikes me that what may be going on here is we have kind of this induced local movement of first instars hence we reap multiple other mechanisms of mortality.

And the selection essentially -- we have a situation maybe -- or driving toward a situation where we don't have much selection at all, hence a perfect -- in a sense, process.

I mean, if you wanted to prevent

resistance from developing, don't select them. And so as I think about this, and think about some of the results you guys are getting, I wonder are we talking about reality here?

DR. PORTIER: Any other responses to this question?

I believe that response was again back to the issue of, do we even need an IRM strategy; did I get that right?

So, I think we're pretty much finished with 2-B. I have a number of points here. I think the main answer in terms of placement of the corn refuges in terms of the types of research that would be needed were basically quantified movement and mating dispersal before and after -- movement before and after mating -- especially in the male, with more emphasis on the adult than on the larvae, especially depending on the strategy that it is going to be used for the placement of the refuge.

Considerable debate about whether to worry about the larva at all and considerable debate about the density pressures that might occur and whether that's important or not, in terms of measuring movement both as a rate and as a movement away from the natal field, and that we have much less expertise on the northern and the Mexican than on the western and that if you are going to focus your effort, focus it on those.

Have I caught most of everything?

Any disagreements with that very brief summary?

I'm sure I'll write up will be much better than that.

Okay. I think finished with 2-B.

Ms. Rose.

MS. ROSE: I just question -- your last statement was that they should focus on northern and Mexican --

DR. PORTIER: Let's say more focused on those.

MS. ROSE: More focused -- I'm more comfortable. Thank you.

DR. PORTIER: Not absolute.

I'm about to announce that we're going to take a break at this point and come back in 15 minutes. The current time is 20 after -- 20 after 3, so we'll come back at 35 minutes after 3.

(Thereupon, a brief recess was taken.)

DR. PORTIER: Welcome back to the FIFRA Science Advisory Panel Meeting.

We have just -- before we get started on the questions again, I'm going to ask the panel how late you would like to go this evening? We had scheduled to end at 4:30 this afternoon.

It does not appear to me that we're going to get through to question 3 by 4:30, and so I want to propose to the panel that we go until 5 o'clock and we finish answering whatever question we are on at 5 o'clock and then at that point we end for the day.

We have half a day scheduled for tomorrow but there really is no adjourning time until we finish all our questions tomorrow.

But at least I want to give the audience and the EPA staff an opportunity to know when we're going to try to finish up today so they can adjust plans as necessary.

Does 5 o'clock -- is that good enough for the panel?

Are there any objections?

Okay. So now if we could go onto question 2-C, please -- 1-C.

MS. ROSE: Question 1-C asks the panel to discuss the panel whether and if so what more information is needed on mating habits of the positional patterns, number of times a female can mate and fecundity, as it relates to refuge structure and placement.

DR. PORTIER: Dr. Weiss.

DR. WEISS: If you will give me time, Mr. Chairman, I want to get down in my computer where I have this question asked so I can -- if I could find it.

DR. PORTIER: While are you looking, Dr. Hubbard.

DR. HUBBARD: This question in my mind is fairly closer related to the previous question and in summary, the primary points that from my mind are larger scale studies on the impact of MON 863, both larval expression and above ground expression on movement -- below and above ground expression on movement of adults and its effect on mating.

My computer is booting as well, but I think that's the bottom line and then many of the comments from the previous point apply here as well.

DR. PORTIER: Dr.Weiss.

DR. WEISS: Okay. I found my spot now, Mr. Chairman.

Looking at it in the context that I think using question A as the leading, comparing this plan for -- that has been developed for westerns and northern and how that relates to the other two species -- southern and the Mexican -- again, I think we know quite a bit perhaps on the mating habits of the western relative to the other three species.

Ovipositional patterns -- I believe we

know quite a bit again about the western where it lays its eggs as far as in the soil, perhaps not as much as field choice, but with related to adult movement. And the number of times a female can mate and its fecundity, again I think we have a relatively -- quite a bit of data on the western corn rootworm.

As it relates to the refuge structure and placement though, I think it is all related to the earlier question when we talked about female dispersal because the female will determine where those eggs will be laid.

In looking at the northern, I think the northern we would know relatively more than we would know about the southern and Mexican.

My concern would be based on what I have read and my knowledge, which is limited on the Mexican corn rootworm biology. So I don't know if we know quite as much, if at all these questions on fecundity in general -- general biological parameters.

So, that's how I would put it in context of I think -- question A leads across this in asking relative to these other two species.

DR. PORTIER: For my own clarity on this, I'm not sure you have discussed how it actually relates to refuge structure in pattern in terms of what research would tell you how these things better relate to that or have we already covered that adequately?

I just want to make sure if we have already covered that adequately.

Dr. Caprio.

DR. CAPRIO: If I could chime in, and this is more based on work that I have done with verisence and helicoverpazea, but in terms of source synch dynamics, if you are talking about these infield refuges and one of those critical factors is females merging in those refuges, where they lay their eggs, what proportion of those end up in a refuge, it plays into the population dynamics of the refuges.

So, you need to know something about the ovipositional patterns of those females that I don't see in the data yet. So it would be hard to determine how large a suitable width of an infield refuge would be.

Again, that's a cotton -- a field cotton person speaking about corn rootworm.

DR. PORTIER: Other comments?

Dr. Gould.

DR. GOULD: Just something we were discussing in this issue of mating habits and the ten-day delay in emergence, it seems like this might be not very important in terms of female fitness but more important in terms of male fitness, because it is a pertangerous (ph) species where the males come out early and the male coming out 10 days later may have lot less opportunity for mating and it would be good to investigate how much that affects male fitness, to have them coming out later.

DR. PORTIER: So the panel feels that we have adequately addressed the question?

I'm going to make it a simple question in terms of the types of research we need to decide whether we use an infield refuge versus a next-door field refuge versus a slightly distant refuge.

We know enough or we've outlined enough research to be able to answer that question or to improve the answer to that question?

Dr. Andow.

DR. ANDOW: I guess I would like to -- on the infield refuge, are we --

DR. PORTIER: Microphone, please.

DR. ANDOW: On the infield, are we only considering the strips case or are we considering any kind of infield refuge in this case?

DR. PORTIER: I think -- as I read the question and, Ms. Rose, I'm sure you will correct me, the question here is what type of research is going tell them whether it is strips or blocks or next door refuges?

Do we already know enough about that or do we need additional research and if so what?

DR. ANDOW: So, you don't want us to consider the seed mixture as a possibility?

MS. ROSE: If you are going to consider that, it is probably more appropriate under the refuge section when we discuss that. It may -- unless have you comments about research natal movement that would relate to that.

DR. PORTIER: Dr. Hubbard.

DR. HUBBARD: It seems to me -- a key question is, are these insects coming up MON 863 going to serve as refuge insects?

If they are, yes, it is possible that we may not -- that the refuge is just kind of an augmenting the self -- the refuge that is built-in there is similar to what has been done for soil insecticide successfully for more than 30 years.

Just as Dr. Whalon suggested earlier, they may have the built-in susceptible refuge right there.

And I think looking at those insects that come off MON 863 and their mating strategies, and the -- of those insects that come off from that mating pairing is sort of a key question in my mind.

DR. PORTIER: Dr. Caprio.

DR. CAPRIO: Can I just make a comment, because I hear this a lot about individuals coming off of a transgenic plant susceptibles as being a refuge.

It is important to remember that when you do this in the modeling and you have a low dose, those susceptibles are part of the selection process or they have gone through selection, even though they are identical.

In a population genetics term, they have gone through a selection and they are very different than individuals coming off of refuge that have not had selection.

They don't -- I think it's a misnomer to call those susceptibles emerging off of a transgenic crop as a refuge. It's a very different concept.

They are the natural result of selection with a low dose and they are something different than refuge insects even though genotypically they may be identical in a population genetic sense.

They are the natural result of the selection process on a low-dose event.

DR. PORTIER: Dr. Gould.

DR. GOULD: Just for clarification, I it is a very important point.

I mean, if you are postulating that somewhere on those roots there are parts of those roots that don't select at all, then Mike would agree with you that it's just like having that insecticide that affects some parts of the roots, where some of the insects supposedly are not exposed to any insecticide at all.

But if we are postulating that all the roots have toxin in them that are affecting the insects, then Mike's point, I think, is an important one.

DR. HUBBARD: Do you think that maybe there are places where they are not selected at all?

DR. GOULD: I don't know about that but I don't postulate that those insects coming off of insecticides have not received exposure. I believe they have. I believe they have received a low dose just exactly analgesics to this situation.

I would have to say that -- we keep talking about that as if there is, but there's not a lot of data on it.

Does anybody know if those insects coming off are delayed in -- when they come off -- the way they are in the corn with Bt?

DR. HUBBARD: In some situations, there is delay.

DR. GOULD: Well, that would certainly support your idea.

DR. PORTIER: Any other comments?

Ms. Rose, have we answered this question?

MS. ROSE: Do --

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: I know that this isn't as important as maybe we would have previously had thought, but I'm just curious how many times do they mate and do we have a definitive information on their -- on the number of times that they -- the westerns and the northern mate.

If so, if they do mate more than once, what is the sperm competition and what is going on there?

DR. WEISS: Mr. Chairman, Mike Weiss.

I think the answer to that, Rick, based on -- if I recall all the reading I have done, unless anyone can correct me, I think females only mate once, that's it.

MS. ROSE: It was in the NCR 46 report that there is a second mating, but that they -- there is significantly less progeny that the progeny from the first mating is most important.

That was actually going to be the point I ask to clarify because, is that important parameter, I guess, for a model?

DR. WEISS: Is that westerns and northern or just westerns?

MS. ROSE: I'm not sure they specify it. I am assuming it was westerns.

DR. PORTIER: Dr. Hubbard, you were on

the panel.

DR. HUBBARD: I believe that would be westerns. I don't think we have that we have that -- I'm not aware that we have that data for northern.

DR. PORTIER: Is that important?

DR. HELLMICH: They do mate more than once or at least some of them mate more than once?

DR. HUBBARD: Yes some. I mean, I believe that there is a second mating but it isn't always the case and that most of the eggs laid are from the first mating.

John Tollefson if you are in the audience, correct me.

DR. PORTIER: Dr. Gould.

DR. GOULD: I just say that the Olstad model went to great lengths to look at all the studies that had been done and actually incorporated a second mating into the model itself with the probability that there would be a second mating based on the data that was available and indicate there was but it really had very little effect. But there were two reasons why it would have little affect. One is it is late in the season, the lower probability, but again, we're dealing with a moderate dose and the impact of that mating structure becomes so reduced in terms of importance, so...

DR. HELLMICH: But if there was high dose it would have probably more affect.

DR. GOULD: If there was high dose, it could but the probability of that mating occurring is lower. So that's why I think it also -- because Dave did look at the high dose and I don't think he saw a major effect of it.

DR. PORTIER: When you say it had no effect, you are implying it had no effect on the placement of the refuge or the structure of the refuge?

Did you have to go back to the refuge?

DR. GOULD: I better go back to the paper, but Dave considered both the infield and the out of field refuge and then he had that in his model.

So, we could go back and check that. It was a good question we can look at it more carefully. In a lot of cases it took so long for resistance to develop, it is not so clear. So, we should look at that again.

DR. PORTIER: Any other comment on this question?

I'm not sure I can summarize this one very easily. Clearly, I think we heard more research on movements before and after, above ground, below ground, before and after mating, post MON 863 exposure would be something that would be useful for all the modeling In terms of the optimal placement of the refuges.

A lot of the comments that pertain to A and B also pertain to here most notedly the lack of information on some of these parameters for the northern Mexican and southern worm.

I think some additional clarification about whether there is multiple matings in the northern -- was at this time northern -- anyway some of the other root worms -- rootworms.

DR. HUBBARD: I'm not sure we have that information. If it modelers, that's something that might be applicable.

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: This scenario that Mark brought up where we have a little bit of feeding and then there is no selection going on and it is the perfect system for resistance management, I'm just wondering if there is ways that that could be tested and there and aren't experiments that should be directed toward that question.

I know it may be a slightly different question, but it is related to that we're doing here.

DR. PORTIER: Is that going to be more pertinent to the question -- the questions tomorrow referring to refuges themselves? Any other answers to this question -- clarifications from EPA?

Let's move on to 1-D.

MS. ROSE: The final part of question 1, the panel is asked to discuss how should corn rootworm extended diapause and oviposition outside of corn -- for example -- should corn-soybean rotation be used to evaluate the effectiveness of IRM plans?

DR. PORTIER: Dr.Weiss.

DR. WEISS: I don't quite know how to start the this question or the answer to this question.

Northern corn rootworms do have extended egg diapause in a localized region, as I understand it in Northwest Iowa, Northeast Nebraska, parts of South Dakota that border those two states and western corn rootworm oviposition in soybean is an Indiana-Illinois phenomenon for that subpopulation.

To me, I don't know quite how we factor this in, quite frankly. If we have a subset of a population, the northern corn rootworm moving out of corn or laying eggs in corn, but that field will not see corn for another cycle, how do we factor that in? What percentage of those corn fields in that area are in that situation where they grow corn in that rotation system rather than continuous?

And western corn rootworm oviposition outside of -- in the soybeans, the question I have there is perhaps Neal can answer is, what percentage of the western corn rootworm population as a whole have that trait?

When you look at a western corn rootworm population in a corn field, which they are emerging, what percentage of that population goes and oviposition in soybeans?

DR. PORTIER: Dr. Neal.

DR. NEAL: We do not know the answer to that in terms of what percentage or how homogeneous or heterogeneous the population is in terms of laying eggs in corn fields versus soybean fields.

The best research is coming out of Joe Spencer's lab in Illinois on this question and he is finding that the females will lay eggs both in the cornfield and outside of the cornfield.

Genetic analysis so far, we have not

found any differences between the adults emerging from continuous corn and adults emerging from first year corn.

DR. PORTIER: Dr. Andow.

DR. ANDOW: It seems to me that there -- that the way that extended diapause or oviposition differences by the western corn rootworm would interact -- first of all the I think that the areas where these are occurring are a bit more extensive than what Mike characterize. So, that it is a bit more of an issue than just a few restricted areas.

But the way that they can interact with the resistance issue is if -- I think primarily through grower behaviors in terms of how the growers decide to implement the different -- different methods of trying to manage corn rootworms.

So, to some extent, I think, this particular IRM issue is tied up with -- to what extent is their crop rotation versus -- and different types of crop rotation, versus use of things in first year versus continuous corn so on.

I think that there is going to be an important component to this IRM plan ultimately, that deals with the decision making behaviors of the farmers. You know, under what circumstances do they tend to do certain things, which then creates the selection pressures or doesn't create the selection pressures.

So, I would suggest this raises a bunch of issues related to how we integrate sort of the economic behavior of growers with the biological selection associated with resistance management.

So, I would say that's a big area and that that would be an area of research that could be quite fruitful.

DR. PORTIER: Any other comments on this question?

Dr. Hubbard.

DR. HUBBARD: I don't have a whole lot to add on this particular question. Although, other than to reiterate there are huge differences across the corn belt between the behavior of adults in Illinois and in Indian, versus Iowa and Nebraska.

In portions of Illinois and Indiana, growers -- as Dr. Andow mentioned, may wish to plant this product in the first year corn. That's probably not going to be the case in any other area even the extended diapause area for the northern corn rootworm.

The one thing that they want -- that should be documented is -- in Illinois and in Indiana it might be possible to be use something of a different crop history as a refuge but I don't think that this is a good idea because it is not a consistent message and it should probably be first year corn. That's the refuge if they decide to plant the product in first year corn.

I don't know if the rest of the panel would agree to that or if there should be an exception Illinois and Indiana. But I think, to me, it looks like a way that farmers could avoid treatment costs in the refuge.

DR. PORTIER: Dr.Weiss.

DR. WEISS: Perhaps we know the answer to this, Bruce and Jonathan. Jonathan, you first.

On a working threshold or treatment guideline for growers, do we have that established in soybeans?

So, if you hit a certain threshold of adult westerns in a soybean field, you know you have a high probability of injury the next year?

DR. NEAL: In Indiana we're currently using yellow sticky card monitoring system. It is based on trapped counts over a seven-day interval. If the total number of beetles caught in a soybean field that exceed the threshold, then we recommend treatment.

DR. WEISS: So, moving forward then, if we -- if we had that -- if growers had that information to base a decision on, whether they used an insecticide or if this product gets registered would be a decision that they could make?

DR. NEAL: That is correct.

DR. WEISS: Bruce, I don't mean to put

you on the spot, but you are closest in geography to my recollection.

Do they have a threshold of northern on corn in the extended diapause area which would then go to the -- not the next crop year but the next year that was in corn for treatment threshold?

DR. HUBBARD: I think that Ken Osley had developed. I believe that's the case.

DR. WEISS: Tully might know.

DR. HUBBARD: Tully, do they have that threshold?

DR. PORTIER: Excuse me.

Let me make sure I'm understanding what you are asking here, because I'm looking at this question, I'm trying to find our answer to the question.

Because as I read the question, it is -- I would have inserted changes in here. How should changes in CRW extend to diapause and oviposition outside of corn be used to evaluate the effectiveness of an IRM plan? In a sense, this is a question about evaluating the effectiveness of an IRM plan, not necessarily designing one.

I think we've been given part of an answer. Maybe I'm miss reading your question, but I think we have given part of an answer here in the sense that the question of a treatment threshold reflects back on whether or not you are seeing changes here and seeing those changes tells you whether or not the IRM plan is working or not -- or have I missed the point?

MS. ROSE: To some degree, but I think we were looking for how is this extended diapause going to effect an IRM plan, not necessarily the changes, but the fact that it occurs in considering that end of development and how it will affect an IRM plan.

DR. PORTIER: So, in terms of the development of a design for an effective IRM plan -- and so we were talking about that?

MS. ROSE: For western and northern.

DR. WEISS: Right. Let me explain my

train of thought, Mr. Chairman.

What I'm trying to get at is unless we can predict with some ability whether a soybean field, for instance, is going to have a significant population of corn rootworms, you have to have that sampling strategy.

If you did not have that, then I can't see what I think would happen is if growers cannot predict that and had this trait available I agree with Dave. What they would do is probably put that in or put a soil insecticide down planting without sampling at all.

But if they know that a soybean field could have injury, then they have a choice to make.

So, what I'm trying to ask too, is do we have that -- if Purdue has developed that for soybean fields, the question that I'm asking on the northern, do we have that same number that we would know if a field was going have significant injury then the grower would decide, is he going to implement a control strategy or not.

If he is an above that threshold he probably would. If this trait was available he would have a choice between this and conventional insecticide, which would mean then that that field could or could not be a refuge. I don't know if you follow my logic, but to me it's --

DR. PORTIER: I have it.

DR. WEISS: So, I guess the question is, do we know what a working threshold is if for northern corn rootworms in the extended diapause area to pull the trigger two years hence?

DR. PORTIER: Do we know that?

Dr. Andersen.

DR. WEISS: If we know that, that's fine.

DR. PORTIER: Ms. Rose.

MS. ROSE: We don't know that information. EPA doesn't have that.

DR. HELLMICH: Would John Tollefson know?

DR. PORTIER: Dr. Tollefson, yes or no? Do we know that; does that exist?

DR. TOLLEFSON: I have a database that would address that question. If you want me to answer it.

DR. PORTIER: Yes or now, that's the answer I'm asking for.

MS. ROSE: Yes; he has the answer.

DR. PORTIER: I think, yes, is the answer.

DR. WEISS: So, we have that -- so we have a way of predicting whether a population is going to be economically damaging in soybeans or in corn grown the next cycle.

So, then that means that that field, in my mind, could be used as a refuge. So -- where am I going with this?

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: We did our Master's degrees together, so we know each other pretty well, so I can do this -- maybe not.

DR. WEISS: Go ahead, Rick.

DR. HELLMICH: I think the question is, if you want to use it as a refuge, how do you qualify the quality of that refuge?

So, you can take from it there.

DR. WEISS: Well, that's what I'm trying to say. So that ground could then be used as a refuge I we know it has a significant population in it.

I don't know how that exactly falls into the effectiveness of the plan, but then, if have you that you know that you would put that additional selection pressure on that population if you wanted.

If you wanted not to put the event selection pressure on that population, then you would go with conventional insecticide or no treatment, but if you did, you would be putting additional selection pressure for not only the extended diapause or oviposition outside of corn, but also the selection pressure against the Bt.

DR. PORTIER: Dr. Hellmich.

DR. HELLMICH: If I was a grower, I think I would try to figure out ways that that could be considered refuge, so, that they could maximize the use of this Bt product. That's one way that they could pursue this.

I think that there will be growers that will want to count that as refuge. And I think maybe the question here is how do we rate that as whether or not it is acceptable or not acceptable as a refuge.

DR. PORTIER: Any answer to that question?

Dr. Hubbard.

DR. HUBBARD: I think to be consistent that the refuge should always be the same as the MON 863, the same whether soybeans the previous year that you are planting your MON 863, I think you should have the same agronomic practices and that's what your refuge should be. That's a consistent recommendation. That's just my opinion.

DR. PORTIER: Dr. Neal.

DR. NEAL: I would like to add that Indiana is very concerned about the spread of rotation resistance among western corn rootworm.

And the strategy you are proposing in those areas where rotation resistance is not prevalent, then treatment would be applied to continuous corn but not to first year corn. Because there is no economic advantage to treating the first-year corn.

Now, if one treats the entire continuous corn but not the first-year corn, then that's providing additional selection pressure for this rotation resistance.

And according to Dave Andow's model on development of rotation resistance, when you exceed 80 percent crop rotation, then that is a strong factor for selecting for this behavior of indiscriminate egg laying that leads to the rotation resistance.

DR. HELLMICH: So, having said that, I would agree with Bruce that we wouldn't want to encourage that that because it probably would have a tendency to select for rotational resistance. That's a good point.

DR. PORTIER: Any other answers to this

question?

Does everyone agree -- could somebody summarize that last point for me, just so I understand it?

If I had to summarize it myself, I would say that what have you said is that the soy shouldn't be used as a reserve and it shouldn't affect placement of reserves within the Bt fields.

Have I caught that? No.

DR. HELLMICH: That's correct.

DR. HUBBARD: I'm not sure I interpreted what you said. My answer is that if you plant in first-year corn your MON 863 -- that's what you are refuge should be. That would be my answer.

DR. PORTIER: If it's first-year MON 863, then the soybean is a proper reserve, but anything else it shouldn't be considered?

DR. NEAL: I would agree with that.

DR. HUBBARD: If you plant your corn in your MON 863 in continuous corn, your refuge has to be in continuous corn.

DR. HELLMICH: Didn't Dave model this a little bit?

Do you know anything about that.

DR. GOULD: I don't have the details to give you on that.

DR. PORTIER: Just so I've got it clear. Everyone on the panel agrees what Dr. Hubbard just -- and Dr. Neal just clarified for us?

DR. GOULD: The only potential place of controversy is whether you should ever have the rotational corn, the first-year corn after soybean ever be a refuge.

And it depends on -- I think David Olstad's model would be good to address that. Perhaps we shouldn't make a complete conclusion on it, but certainly at least what you just said, because you are certainly going to -- it depends on how much rotational resistance matters in your area.

If it matters to you a lot, you really shouldn't do it. I think John Neal's comments are right on. DR. PORTIER:

Okay. Does that answer the question for you?

DR. ANDERSON: We just might have a clarifying point from have read the models.

MS. ROSE: The only clarification having read the model when I presented this morning was that I believe his model showed that the extended diapause didn't have an effect.

But that's just one model that has -- we wanted the panel to elaborate, but if you are asking what his model should --

DR. GOULD: Didn't have effect resistance to Bt developing or didn't have an effect on stronger diapause delay?

MS. ROSE: The time to resistance.

DR. GOULD: What Jonathan Neal is talking about is that if you do this, you are going to select for more diapause resistance.

MS. ROSE: And that I'm not sure if it addresses.

DR. GOULD: No, and that's a critical point to bring up.

MS. ROSE: Thank you for clarifying.

DR. ANDERSEN: We're ready to go on.

DR. PORTIER: Okay. If we could go on the to 2-A.

MS. ROSE: The next section relates to dose and there are two aspects to this question.

A, states the panel is requested to comment on EPA's determination that MON 863 expresses a low to moderate dose for corn rootworm.

The panel is requested to provide guidance on definitions of a high, moderate and low dose for a corn rootworm protected Bt corn product.

DR. PORTIER: Dr. Caprio.

DR. CAPRIO: All right. That seems to be a reasonably easy question. I don't think it I will get argument from anyone that it's not a high dose.

As far as defining moderate versus low dose, is there any real line of demarcation that you could safely say -- I think Nick Storer's figure that he had this afternoon where he looked at dose -- unfortunately, it only went down went down to 50 percent, but obviously there was a clear line of demarcation between high dose and something that is say -- 90 percent, that would be a worst case.

He is correct that somewhere after 50 it drops off to zero and whether or not that's a very sharp point, I don't really know. But I don't think that there is -- the question in my mind is more, is it a high dose or did it just miss a high dose.

The last thing you want is 90 percent mortality rather than 95 plus percent mortality because you won't get the benefits of the high dose but you will get strong selection.

So, I'm less inclined to make any comment or distinction really between moderate and low dose, but rather to me, the important distinction seems to be between high dose and not quite a high dose.

DR. PORTIER: Dr. Andow.

DR. ANDOW: I have to say I agree, but I

would like to -- just to make sure I would like to ask the EPA.

Is there any reason that you have for trying to make a distinction between low and moderate dose?

MS. ROSE: Only if it would affect refuge size and structure.

DR. ANDOW: I don't see any clear line of demarcation, so, I would like to reiterate. And just to complete the record -- well, I have always said that the operational definition of high dose is flawed.

MON 863 is no where near the demarcation line, so I don't think it would be of any benefit to reopen that discussion at this time.

DR. PORTIER: You are saying then that once are you out of high dose, the operational dose of low to moderate doesn't really affect the IRM plan?

DR. ANDOW: What I've said is that I can't think of any reason why we should make that distinction.

DR. PORTIER: Dr. Federici.

DR. FEDERICI: I don't really -- I agree with the two previous speakers. I don't have anything to add. I agree with them

DR. PORTIER: Dr. Neal.

DR. NEAL: I concur. It is clearly not a high dose because of the large number of beetles that are emerging.

Certainly, I think a relevant question to be asked here is does the use of MON 863 effect the gene frequency of the population with regard to resistance of the individuals and how great is that a factor?

DR. PORTIER: Dr. Gould.

DR. GOULD: I agree completely that there is no demarcation between a low and a moderate dose.

I don't think that is necessary to draw. I don't think anyone would disagree if you had 80 percent mortality versus 5 percent -- well, fitness different, not even mortality, that that's a big difference in terms of resistance management.

I think something that Mark was bringing up, I think pertains to this and I think should be addressed.

I think what you were saying -- almost throwing the your hands up saying, well, gee, there isn't any selection at all here.

So, I think that although you can't demarcate, because every variety in every own environment is going to be somewhere between zero percent selection and maybe 80 percent selection, let's say.

So there is no use in calling -- putting in it a category. I think I agree with you, you can't put in it a category, but we better be very aware that we do want to understand what is the selection intensity of each crop we put out there because it pertains to resistance.

It is a dramatic effect on resistance. I guess what I would say is that in terms of this situation, we need to look at it when we're talking about how big does the refuge have to be.

We need to be able to figure out what the selection intensity in the crop is. And that I think is more important. We're not going to have a category but we should be able to do the research to tell you what the selection intensity is.

DR. PORTIER: Any other comments?

Does that answer the question?

Everyone agreed. I'm not going to reiterate.

Dr. Hellmich.

DR. HELLMICH: My only question is, is this where we should open up the discussion about the selection intensity like Fred is saying or should we wait until later, determining whether or not this -- if there is any selection going on with these events?

We talked about that before and we were going to delay it until refuge -- refuge, that's fine.

DR. WHALON: Actually, I think it fits under dose, because if you can't generate selective dose, I mean, you can in first instars, obviously, but not beyond that. And even in first instars, it is difficult for a lot of technical reasons and for over growth of plates -- bioassay plates and things like that.

So, the whole issue of trying to determine selection intensity which is crucial to resistance management has its base in being able to do dosage mortality or at least some assessment based on dose.

DR. PORTIER: Does the panel basically agree that selection intensity is something critical to be measured prior to doing an IRM?

Is that what I'm hearing and is something else we want to say on that?

How accurate should we be in estimating selection intensity? Scientifically, what would you suggest in terms of its impact on the IRM plan?

Dr. Andow.

DR. ANDOW: I think it is a very important parameter. I think it is not that hard to measure because selection intensity -- it's hard in one aspect but not in another. Selective intensity has two components.

It's related to the advantage of the heterozygote and the advantage of the homozygote recessive -- resistant types, if we're looking at a single gene type model.

So, that means that if you estimate the mortality rate of the SS's when they are exposed to the Bt plant versus when they are not exposed to the Bt plant, you have an idea of the additional mortality that the SSs suffer as a consequence of being exposed. That you can take as a first estimate of the selective differential associated with those two. Then the rest is sort of up to how strong is heterozygosity, which we don't know, so, we just have to assume different levels and work with that.

But essentially, if you estimate efficacy, a good estimate of efficacy will give you a good estimate of the selected differential.

DR. PORTIER: Does the panel agree with that?

Dr. Gould.

DR. GOULD: I think that's a good first starting point, but I think all the studies also show that sublethal affects can have more of an effect on fitness than just the mortality estimate.

So, while I think we should never stop right there, especially with these corn rootworms where we have delayed emergence. I think there are a lot of other fitness components you have to look at.

But, I agree with David, it can be done.

DR. PORTIER: So, based on the models that we're using and the relative effects of changing the efficacy -- let's stick with that for a minute.

How accurate do you have to be within what? So, here we're looking at something where the efficacy has been described as being between 20 and 60 to 70 percent, depending on a lot of variables, maybe.

How accurate do we have to be?

Dr. Caprio.

DR. CAPRIO: Again, I just think of the graphs that Nick Storer put out the rate of increase. It was relatively insensitive from 90 percent down to 50 percent.

I don't know enough about it to know -- I haven't really looked at curves that go beyond that, but just based on that figure it would say it is not particularly sensitive to that parameter.

DR. PORTIER: Dr. Gould.

DR. GOULD: Again, I have to agree and disagree with you. I mean, the reason that Nick's model -- thing looked like that was because the high dose really works and you had a huge drop off there and therefore, the scale got diminished.

What Nick was looking at -- and I think Dave brought this up, if you looked at that scale it was on log scale because of that.

So, it looks very diminished but it is

not quite so diminished it if you look at it in absence of a high dose.

It gets back to the fact that we're playing games here with very small advantages in resistance management when you have a very small refuge of 20 percent and a low to moderate dose.

Of course we're stuck a little bit. But if you look at that I think you will see at least the difference of 10 percent in terms of fitness is going to matter.

But it depends on EPA and how sensitive they are to how many years they want the product to last.

DR. PORTIER: But that refers to fitness and I was going come to that in a minute. But on efficacy, would you agree that knowing it is less than 90 percent is enough and then go to fitness?

DR. GOULD: If you want to make -- knowing that it is less than 90 percent is enough to know that you have to measure other components of fitness -- I would say that's true.

I mean, I would say -- I would go up to

95 percent you better start doing that, but that's fine yes.

We could discuss this in detail because it is something that is something that is a mathematical issue. You have to -- we're going to get pretty vague here.

DR. PORTIER: Dr. Andow.

DR. ANDOW: I'm going to pass on your particular question.

DR. PORTIER: Any other comment on that particular question that is different?

DR. WHALON: I just surmised that when you get into that part of an efficacy line, I think that you are looking at a stochastic probability and the inference with the noise that is around it is really difficult.

The question you are asking is really open ended given the kind of data that is available.

DR. HELLMICH: I guess my question is can we measure selection intensity without having resistance colony identified? It seems like maybe that can't be done.

If that is the case, I mean at some point I think we talked about whether or not we should be selecting for resistance colonies. That would suggest we should be.

DR. PORTIER: Dr. Andow.

DR. ANDOW: I guess, like I was saying, a major component of the fitness differential is efficacy. Right there you have a first order approximation to your parameter.

And then if you want to deal with the heterozygotes, that usually -- because if they are dominant then they contribute just as much. But if they are dominant you just add them in and you've got your answer.

It is sort of like -- and then the added fitness factors are going to modify that as well. But you are going to be pretty close with just an efficacy measure. And it's probably going to be maybe a little bit higher than that in terms of the actual fitness differential.

DR. PORTIER: Dr. Gould.

DR. GOULD: I just want to just make sure this is clear for Rick. I do think that you can get very far without having a resistant colony and I agree with Dave except I keep saying you have to go beyond the -- just the mortality.

This has been done in the past and used in the modeling efforts -- is coming up with scenarios based on just how much the susceptible one has been decreased in fitness without having a resistant colony.

You can make the assumption as Bruce -- how does this colony -- he's day, well, that wasn't completely resistant. So, he assumed that its fitness was also decreased compared to non Bt things.

So, you could work it pretty well without having a resistant colony.

And to get at Mark's stochastically, I think that does make the challenge greater. I think we have seen with the corn ear worm where we have a moderate dose. We already have information in the field that shows us that it is difficult.

Australia had a worse problem because some of the fields early on weren't putting any selection pressure on at all or something like that, but in the United States, you do see variation in the selection intensity for the corn ear worm in terms of Dave's kind of measure of efficacy.

You will see sometimes where you have 95 percent mortality of the larvae and other times in different fields in the same general area only 60 percent mortality. But in the case of that situation, you can get around that stochasticity by reps and it's been done.

DR. HUBBARD: One question I have for the panel on this is what is actually causing mortality -- how important is it that it's actually the MON 863 event that is causing the mortality versus some extended life -- finding the host, avoiding good feeding the sites -- if that is causing the mortality and it may not be -- MON 863 might not be providing selection criteria.

How important is that?

DR. GOULD: I would like a chance to answer that.

DR. PORTIER: Dr. Gould.

DR. GOULD: I think this is really important question and it comes up again and again. Is it -- does it have to be the directed effect of that toxin on the insect survival?

And we did modeling awhile back on the interaction between partial resistance very similar to this that slowed down growth of elaborating capitellar and impact of parasitoids.

So, we were doing a system where there was only 10 percent decrease in fitness due to the plant itself -- due to the toxin and where that came in, was it slowed down the growth. By slowing down the growth, it led to the window of opportunity for that parasitoid to double.

So, what happened was that the parasitoid was exerting indirect pressure for adaptation to the resistant crop. And in that model, we show very clearly that the adaptation occurs more quickly to the crop when a parasitoid is there versus not there. We did field studies on a parasitoid in North Carolina on the tobacco bud worm. Based on the data collected, looking at this whole fitness differentials, we were able to show that resistance involved five times faster in the presence of that parasitoid than without it.

I think we can show you how those indirect effects -- not direct toxin effects can have an effect. If it interacts with soil moisture, you can have that the same thing.

If the rootworm is taking longer to establish on that crop and therefore when it is low soil moisture they desiccate, that's going to have that same impact of selecting for resistance.

DR. PORTIER: Dr. Andow.

DR. ANDOW: I think it is important to understand what is being estimated is a selection differential.

How the population responds to that selection differential is going to be related to the underlying genetic structure that gives rise to the resistance.

In the case that Fred was talking about, if you have a single allele, it doesn't really matter whether or not the trait sort of exposes you to whether you -- do you die of starvation, whether you die because are you toxified or whether you die because you wonder wander off and somebody else eats you.

If it is because you have that gene that you did that, then you get selected for it. So, that's a single gene case.

But if we think about the possibility that there are multiple genes involved here, then when you think about selected differential you can start thinking about the response to selection in the population and then that's going to be related to the underlying genetic architecture of the response.

So we can sort of more generally deal with this problem I think in the low dose cases, which we have to be thinking about -- multiple alleles, quantitative traits as well.

So I think that this is really good -- that's why it is so important to focus on the selection differential especially in these low-dose cases.

For example, if it's a quantitative trait and there are multiple alleles involved, then are you going to have a different kind of response to selection and then the evolutionary process is going to proceed in a different way.

DR. PORTIER: Dr. Whalon.

DR. WHALON: Well, I guess maybe I'm always recognizing ironies, but it seems like we have a field selection process that is very akin to historically what has happened in the laboratory all the time when you have a quantitative trait selected because of how you manage a selection process, essentially in the field.

In this case, with this Bt thing or at least that's what we're hypothesizing. It introduces a lot more difficulty in trying to actually determine what a refuge ought to be and what strategies ought to be to manage effectively, resistance.

DR. PORTIER: Any other comment on this question or additions to it?

So, the first half of the question -- at least I think the answer there was pretty clear, that the panel agrees with EPA's determination that it is in this low to moderate range.

I didn't hear any disagreement with that and when it came to identifying the classes and the criteria for identifying classes, again the point from the panel was that two classes is sufficient for this issue -- high versus everything else, although zero would be treated differently -- zero efficacy would be treated differently.

Then considerable discussion about selection intensity and the direct measurement of selection intensity and its importance in the IRM management in cases when are you below the high-dose effect compounds.

Dr. Caprio.

DR. CAPRIO: I guess I was just going to mention that -- or still say that there is this rather ill defined category of almost a high dose that is substantially different than a moderate or a low dose, that if you aim for the high dose and don't quite make it, that's a product that I would seriously have questions about -- how to deal with it.

So, I think to say that there is just two categories. I think there is a third worse case scenario that the EPA might want to keep in mind.

DR. PORTIER: So, would it be fair to characterize then, that in cusp area -- let's call it 90 or 85 to 95 percent mortality, that the accuracy is more important in estimating that number than it is in the lower area and that that would play an important role in the IRM plan.

Is that what you are telling me? Because the question is sensitivity to the IRM plan and how you would manage it. You were saying that you are not sure how you do it in those cases or it would be much more difficult.

So, in that case, you would want to be certain you are in this cusp area, which means much more accurate estimate of the efficacy.

I guess, yes because you might not want to let that product proceed so you want -- before you did that, you would want to know fairly precisely what --

DR. PORTIER: Dr. Gould.

DR. GOULD: Just to comment, I think we want to be careful that we recognize what came out of the 1998 SAP meeting in terms of definition of high dose and what we call "close."

When you say, 90 to 95 percent mortality, you are talking about the susceptible insects. That would be considered maybe getting into that cusp, but we're talking about the definition that we're using right now and is in this document -- do we agree with a 25 fold level needed to kill 99 percent of the susceptible?

So, that cusp then, are you including all the way from 90 percent to 10 times that or 25 times?

I think we better be careful in trying to answer that. I thought Dave did a good job of not answering.

Because it's a very difficult one to deal with and I think when we start dealing with population dynamics, not being that close could work out pretty well looking at some of Nick's results.

I think we need to be very careful. I do agree there is that category of not quite. I'm not sure how you want to label it.

DR. PORTIER: But could we actually just refer back to -- in our earlier report, the earlier '98 report that deals with the tissue in more detail?

DR. GOULD: It doesn't deal with the not quite situation.

DR. PORTIER: Dr. Andow.

DR. ANDOW: What my response was is that while there are issues associated with that border line -- that definition of what high dose is, I think that the way I would like to see it in this report is that it is going to do us little good in the consideration of MON 863 to revisit that issue.

DR. PORTIER: Okay. I think that's clear here.

Does everyone agree with that?

Ms. Rose.

MS. ROSE: As have you said, I have heard that we have high dose or non high dose product and didn't see a need to distinguish between low and moderate and I notice that we didn't ask a question like this under the Model section, so I would like to ask it now. When dealing with a non high-dose product such as MON 863, then what would be the input parameter for percent survival?

If we're not going to actually define it, how would we deal with that?

DR. GOULD: You put it in, based on imperial data on what the survival is. But you are better off putting fitness in stead of survival. I think all the model benefit by putting that kind of thing in.

I think all the models that are spatially explicit and have overlapping generations and such can handle these moderate-dose plans that delay development. That decreases fitness.

Other factors like that, I'm sure that the other modelers will comment on that.

DR. PORTIER: Dr. Andow.

DR. ANDOW: I'm not sure I completely understood your question.

MS. ROSE: For instance in Monsanto's modified version of your model, Mike Caprio, they define the low doses as greater than 50 percent survival and the moderate dose is greater than 30 percent. There was a slight difference in the time to resistance by changing those numbers.

So, without having a number to put into these and leaving this so open ended, I guess I see a little bit of a concern of being able to really determined the timed resistance.

DR. ANDOW: I have looked at some of that information. But certainly not all of that. And there are slightly different rates of egg applications.

So, part of the variation survival is probably relate to that. So one has to look at the relation between density dependence and the effects that density dependent mortality has on the estimation of survival of the initial Bt crop. So, it does start to become a little bit more complicated.

But suppose you were to do several trials and you still got that variation.

I think then what one would want to do is one would want to -- in the models one would probably want to see -- you would probably want to see results that are related to the mode or mean of that distribution as well some of the extremes.

Just to make sure that if it did turn out that on average it was much higher or lower than the mode or mean of the experimental efficacy trials you are still covered.

DR. PORTIER: Can I ask a follow-up question on that?

While I believe there is a change in time to resistance, is there a change in the optimal strategy for IRM, yes or no if you change in that range of 70 percent mortality to 40, 50 percent mortality.?

Dr. Caprio.

DR. CAPRIO: I'll just say it probably won't change the strategy, but it might change the proportion of refuge. In other words, how you deploy that strategy.

DR. PORTIER: So, it could have an effect of some sort?

Dr. Gould.

DR. GOULD: I concur with that. If EPA decides that they want the resistance management strategy to last for 15 years, given that's what you want, then you might wind up with -- at the 60 percent mortality, having the refuge have to be 60 percent of -- and if it was 20 percent mortality that refuge may only have to be 40 percent of the to get that 15 years.

So you would indeed change what would be the strategy if you had a notation of where you want to end point it.

DR. PORTIER: Is that clear now?

Can we now go onto 2-B? The panel agrees? Yes.

DR. ROSE: 2-B asks the panel what techniques should be used to determine dose for Cry3Bb1?

DR. PORTIER: Dr. Hubbard.

DR. HUBBARD: My suggestion on this question is we ask the world expert who is in the audience, Dr. Blair Sigfried.

DR. PORTIER: Dr. Weiss.

DR. WEISS: Am I on this question?

DR. PORTIER: Yes. I avoid including the audience in these issues for a lot of reasons. I guess I'll just make that clear at this point.

EPA goes to a lot of trouble to try to balance the panel in terms of a lot of issues.

And part of what the -- because we don't try to reach consensus, we're seeking -- the EPA is seeking the end point from the individual panel members.

I prefer not to have that influence by the audience except during the public comment period. If we really have to go to the audience for a particular clarification question we will, but I'm not going to go for the audience for an answer to -- a direct answer to one of EPA's questions.

Dr. Weiss.

DR. WEISS: Mr. Chairman, I would ask Brian to comment on this, because I think -- of the panel he has probably the most experience in this area.

DR. PORTIER: Dr. Federici.

DR. FEDERICI: Well, while I look at these various options here and I have to refer back to the talk that was made this morning by the Monsanto -- I don't have his name right here, but Ty I believe was his first name, Ty Vaughan. I assume what you mean here is to determine -- the EPA question is to determine what you would refer to as the LD50, the LD95, that data. Is that what we are really being asked for here?

MS. ROSE: Actually, if you will look at the set of questions that we gave you, what we did to try and inform the panel is provide you with the text from the 1998 one, where they actually came up with different approaches to determining the dose.

In that case, they were following a definition and we decided not to establish a definition in this case.

DR. FEDERICI: From the description of how the bioassays were done this morning, there are better systems, I think, for producing these proteins so that they use an ecoli system, but there is actually available a Bt system that produces very high amounts of Cry3 proteins.

Now, I can't say for sure it would work here. But the levels of protein that they were talking about are very easy to produce with other expression systems. And even if you only have an effect against the first instar, you could measure very accurately with these systems an LD50 and an LD95.

Now, I say LD50, LD95 -- from what they described this morning, you use the term, dose, here, it is really a concentration because from the description of the assay, they are not really feeding on a specific dose per se they are in a milieu of media of some sort and the toxin has been added to that.

There is another thing that came up -- when you go to the plant as suggested in these -- I don't consider any of these satisfactory that were provided as examples, because I think there are better systems.

I want to be a little careful, because I have never worked with a corn rootworm and I sort of get the idea that it is kind of a difficult insect to work with.

But if eggs are readily available, even if only from the field and not from colonies, and you are just dealing with the first instar, I think you should be able to measure a range of doses and actually get regression lines for the LD50 etcetera. I would call it again an LC50.

There are systems that have been developed for lepidoptera where you could actually, by incorporating dyes into the toxin mixtures, and then measuring those -- for instance in first instar caterpillars, even small ones, you can get a correlation between the length of the color in the gut and the concentration of toxin.

So it may be conceivable to actually develop an LC -- an NLD FD and LD95.

Having said all that, I'm assuming that the people at Monsanto must know about all this literature because they do a lot of work with a lot of doctors.

So, they be sitting in the audience saying this yo-yo, what does he -- what is he doing? He probably doesn't know anything about the corn rootworm. So I don't like any of these things here.

The other thing that came out of the talk this morning is, it wasn't clear to me and maybe I should have asked the question then, what the actual toxin is.

Is this a pyrotoxin or by the time they got done with their purification, is it the activated toxin? Do you know that?

DR. ANDERSEN: Well, I think John Kough knows that, but I don't see him in the audience. Does -- can Monsanto answer that question?

DR. VAUGHN: We have actually done the bioassays with the full toxin as well as the trichinized truncated toxin and we find no difference.

So, when we typically try and wet up new bioassays, we want to use the most purified form we can get and trypsinizing the protein helps us to get there.

So, in many cases we -- once we have identified proteins in this way we do trypsinize it just to keep the bioassays clean.

DR. PORTIER: Thank you very much That

was Dr. Vaughan, Ty Vaughan.

DR. FEDERICI: Before you leave, just to get some further clarification, if possible, you are expressing -- the corn expresses the pyrotoxin; is that correct?

DR. VAUGHN: The corn itself is expressing full length.

DR. FEDERICI: The full length?

DR. VAUGHN: Yes.

DR. FEDERICI: So, then I would say if you use one of these other expression systems and maybe have you tried them they don't work for you for this particular protein -- I don't know, but for Cry3 they are very good at other expression systems. Then I would say you go onto look at the later instars and you could -- you wouldn't have to be stuck to the first instar.

As I said if you can get very concentrated amounts of toxin, you should be able to -- I would imagine that the second and third instar would be sensitive to the toxin despite the data that you provided here.

I don't know, it's a rather circuitous -- once you have that, then you can calculate what a 25-fold factor is.

DR. PORTIER: Dr. Federici, could you keep a little more focused on the microphone. You are going in-and-out.

DR. FEDERICI: Oh, sorry.

So, in other words, if this system -- if these systems would work where you actually get a concentrated dose even if it is an LC50 that you are determining, you should be able to determine to that -- for I would say the first and at least the second instar what a 25-fold dose is of the LC50.

I hope I have been clear, but if not I'll be happy to answer any.

DR. PORTIER: Dr. Weiss has informed me that I had a bit of a senior moment here. I was going back to lead answers for the first question, instead of going to lead answers for the second question. I do apologize for that.

Dr. Caprio.

DR. CAPRIO: I guess, as I look at this, I wasn't clear if EPA was asking for something specific for this.

And I guess it does say this product -- we're not really talking about how one should evaluate other corn rootworm products. And I don't work with this insect in the lab, so it is difficult for me to evaluate these possible evaluations.

DR. PORTIER: Dr. Andow.

DR. ANDOW: So the question I think is really not so much trying to determine the dose as much as how do we characterize is this a high dose or not, because that's the key piece.

And so how do you show that it's not -- that are you not getting survival at 25X to LC99 and if you know LC50 is really close to the expression level of the plant, then it seems like you already got it right there.

If you wanted more, if you have an SS survival rate that is anywhere in the range that we're talking about, that is a lot less than survival rate of 0.001, which is what you would expect from an LC99. So, you have it right there too.

DR. PORTIER: Dr. Neal.

DR. NEAL: Earlier this morning, I think we were presented with that information at least to my satisfaction as to what the dose was in the plant. The question -- a lot of this question asks us specifically for methods of determining high dose.

And since it is very, very clear that this is not high dose, then there is not a lot of scientific point to determining a high dose, because this product is never going to meet that.

So, I guess I see a lot of this as being relevant to the Bt corn for corn bore, but not nearly as relevant to the corn rootworm.

Now, Brian mentioned the possibility of doing LD5s with corn rootworms and that is possible.

I mean, you can get first instar larvae to imbibe sugar solution, for instance, with dye in it. As much of the Bt as you could get in that water droplet you could feed it directly to the corn rootworm larvae. That would be one way of determining what the high dose is.

But it seems like a moot point because the product is not a high-dose product and they are not attempting to make a high-dose product.

So, unless there is an attempt to make a high dose product, then really you don't need to pursue this.

DR. PORTIER: Dr. Hubbard.

DR. HUBBARD: The one point where I think that this is important is going to be in monitoring. I think that this is -- the method that you determine dose is probably going to be the method that you end up using to monitor, whether you have resistance in subsequent years.

And so, if it is just a simple dose response curve we say that and then that's what may be used in monitoring as well, because I don't know that we are going to be able to do that from large roots or damaged roots or -- I think you are actually going to need to look at the response of the larva to this product in order to monitor whether it has had any resistance.

So, the importance of this question is probably more in terms of monitoring.

DR. PORTIER: Any other responses on this question?

DR. NEAL: I would agree with Bruce's point. I think we need to take that up in the monitoring section.

DR. PORTIER: That was Dr. Neal.

Six minutes to five. Do we go onto question number three?

I don't know how long our answers will be. Dr. Caprio, Dr. Andow -- is it perceived that there is going to be considerable debate on 3-A, B, C, D?

DR. CAPRIO: I submit with this panel, I don't think you are going to escape it on this issue.

DR. PORTIER: That's pretty much what I was going to say. I think there's enough points in here that might be taken up that -- I think we'll make an executive decision here and I think we'll delay the discussion of 3 until the morning, since there's so much related issues associated with A, B, C, D.

I think it would be more appropriate for us to take it as a whole, rather than piecemeal it now, because I can't see us getting through all four parts of 3 before eight o'clock tonight.

Does the panel disagree?

DR. GOULD: I want to make a comment. I asked the folks in our support group to Xerox something for this discussion. I want to make you aware of it.

Early on I thought I was going to be involved in this question. I thought for homework what we needed to have before the meeting was a comparison of all the models. I have drawn up a table that has all the assumptions of each of the four models. I haven't been able to fill it in completely, but I hope we can enter that into the discussion into our panel meeting so we have something in front of us.

So, again, tomorrow morning I hope to have that ready for you.

DR. PORTIER: That would be great.

Before we close, any other comments by the panel on what we have covered up to this point? Any additional questions from EPA?

MS. ROSE: Not right now; we'll talk tomorrow morning.

DR. PORTIER: Mr. Lewis, any administrative issues.

MR. LEWIS: Thank you, Dr. Portier.

Just in terms of our agenda for tomorrow you will note that we are still going to continue working on question number 3.

So for our agenda tomorrow, we have a full day available. We originally thought we were going to end about lunchtime, but we have the whole day to work and we will use the time available to address all the questions.

In terms of handouts from the panel, we actually have three documents we're giving you.

One is what Dr. Gould mentioned about his model comparison. Another is a paper that Dr. Storer is making available to the panel available in the public docket and third is additional data that the Agency is making available.

I don't think we have all the copies made right now. Dr. Portier, if you prefer, we can make this available at the front desk of the hotel when the photocopying is made for the panel. You can stop by and pick it up?

MR. LEWIS: So, you already have two out of three?

If the panel can convene in the break room in about 10 minutes that will make all the deferred copies available.

We'll have the last copies made in about 10 minutes. They can meet in the break room about -- lets make it at 5:10. Panel, we'll give you the final copies go from there.

DR. PORTIER: Thank you Mr. Lewis.

Dr. Anderson, did you have anything to close this out with?

I haven't closed this meeting yet.

DR. ANDERSON: Have a good evening.

DR. PORTIER: Thank you very much.

Again, thank you all for your deliberations today and your patience. Lets close.

(Thereupon, the meeting adjourned at 5 p.m.)

CERTIFICATE OF STENOTYPE REPORTER

I, Frances M. Freeman, Stenotype Reporter, do hereby certify that the foregoing proceedings were reported by me in stenotypy, transcribed under my direction and are a verbatim record of the proceedings had.

____

FRANCES M. FREEMAN

I-N-V-O-I-C-E****   ****I-N-V-O-I-C-E****

FRANCES M. FREEMAN
43773 Sunset Terrace
Ashburn, VA 20147
703/726-6944

TODAY'S DATE: 9/13/02

DATE TAKEN: 8/28/02

CASE NAME: fifra sap

DEPONENTS:

TOTAL: -- PAGES: 408

ATTORNEY TAKING DEPO:

COPY SALES To:

DELIVERY:

COMPRESSED:

DISK:

E-MAIL: no

EXHIBITS:

TRIAL DATE:

**SIGNATURE: